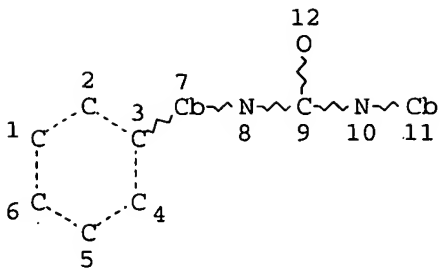


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ENTER (DIS), GRA, NOD, BON OR ?:end
L1    STRUCTURE CREATED

=> s l1
SAMPLE SEARCH INITIATED 11:04:23 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -  22417 TO ITERATE

  4.5% PROCESSED    1000 ITERATIONS                                  0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       439381 TO   457299
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA SSS SAM L1

=> batch l1
ENTER BATCH REQUEST NAME OR (END):sss
'SSS' IS NOT A VALID BATCH NAME
Enter the name you wish to use for the BATCH request.
The name must:
  1.  Begin with a letter,
  2.  Have 1-12 characters,
  3.  Contain only letters (A-Z) and numbers (0-9),
  4.  End with /B,
  5.  Not already be in use as a saved name, and
  6.  Not be: END, SAV, SAVE, SAVED, or an L#.
ENTER BATCH REQUEST NAME OR (END):CC692559/b
ENTER TYPE OF SEARCH (SSS), CSS, FAMILY, OR EXACT:sss
ENTER SCOPE OF SEARCH (FULL) OR RANGE:ful
QUERY L1 HAS BEEN SAVED AS BATCH REQUEST 'CC692559/B'
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=> activate cc692559/a
L1              STR
L2           18 SEA FILE=REGISTRY SSS FUL L1

=> d scan

L2    18 ANSWERS   REGISTRY  COPYRIGHT 2005 ACS on STN
IN    Urea, N-[3-(4-methylphenyl)tricyclo[3.3.1.13,7]dec-1-yl]-N'-
      tricyclo[3.3.1.13,7]dec-1-yl- (9CI)
MF    C28 H38 N2 O
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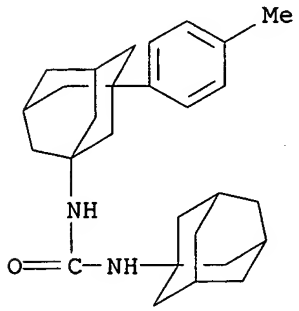


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                0.43       0.64

FILE 'CAPLUS' ENTERED AT 06:58:54 ON 30 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 30 Jun 2005  VOL 143 ISS 1
FILE LAST UPDATED: 29 Jun 2005  (20050629/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

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L3 17 L2

=> d bib abs hitstr 1-17

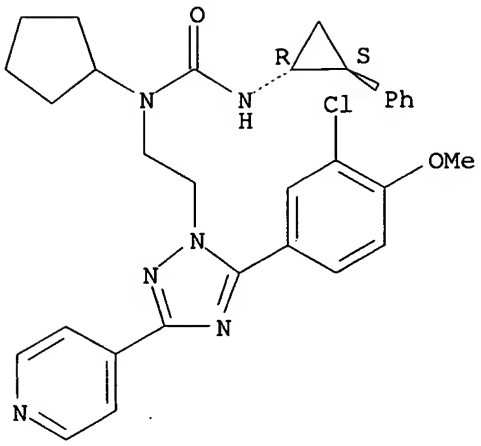
L3 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:902086 CAPLUS
DN 141:388753
TI Heterocyclic compound modulators of Tie-2 and other kinases, and therapeutic use
IN Chen, Jeff; Dalrymple, Lisa; Epshteyn, Sergery; Forsyth, Timothy; Huynh, Tai; Leahy, James; Mann, Grace; Mann, Larry W.; Ridgway, Brian; Sangalang, Joan C.; Takeuchi, Craig
PA Exelixis, Inc., USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004091480	A2	20041028	WO 2004-US10626	20040408

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-461471P P 20030409
OS MARPAT 141:388753
AB The invention provides heterocyclic compds. for modulating protein kinase enzymic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. Compds. of the invention inhibit, regulate and/or modulate kinases, particularly Tie-2. Methods of using the compds. and pharmaceutical compns. thereof to treat kinase-dependent diseases and conditions are also an aspect of the invention. Preparation of triazolyl compds. of the invention is included.
IT **783327-32-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic compound modulators of Tie-2 and other kinases, and therapeutic use)
RN 783327-32-2 CAPLUS
CN Urea, N-[2-[5-(3-chloro-4-methoxyphenyl)-3-(4-pyridinyl)-1H-1,2,4-triazol-1-yl]ethyl]-N-cyclopentyl-N'-[(1R,2S)-2-phenylcyclopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:875033 CAPLUS
DN 141:332214
TI Preparation of quinoline, tetrahydroquinazoline, and pyrimidine derivatives as MCH antagonist for treatment of CNS disorders
IN Sekiguchi, Yoshinori; Kanuma, Kosuke; Omodera, Katsunori; Busujima, Tsuyoshi; Tran, Thuy-Anh; Han, Sangdon; Casper, Martin; Kramer, Bryan A.; Semple, Graeme; Zou, Ning
PA Taisho Pharmaceutical Co. Ltd., Japan
SO Eur. Pat. Appl., 586 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1464335	A2	20041006	EP 2004-7651	20040330
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
	EP 1464335	A2	20041006	EP 2004-7651	20040330
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
PRAI	US 2003-458530P	P	20030331		
	US 2003-495911P	P	20030819		
	US 2003-510186P	P	20031009		
	US 2003-530360P	P	20031216		
	EP 2004-7651	A	20040330		

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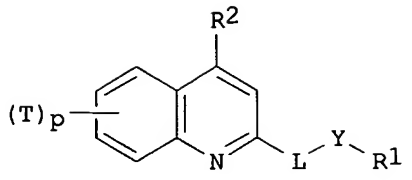

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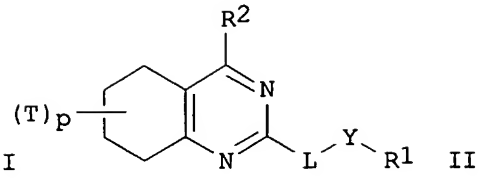

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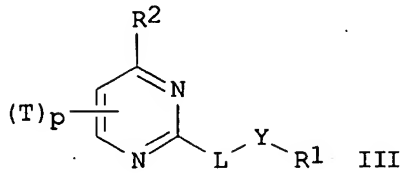

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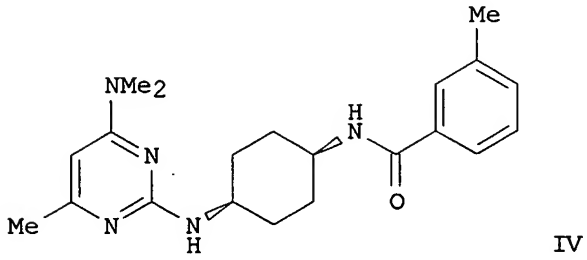


IV

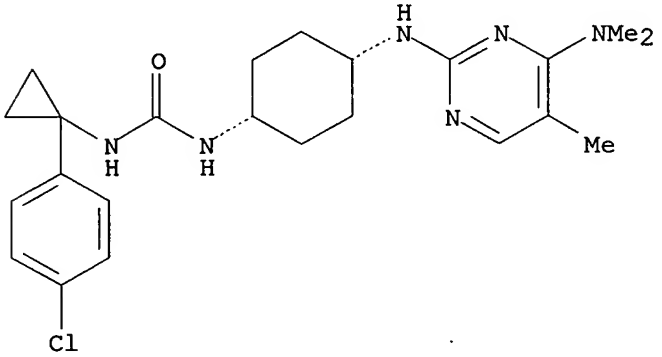
AB Title compds. I, II, and III [wherein R1 = (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl; R2 = H, halo, OH, carboxy, carbamoyl, amino, (un)substituted alkyl, alkoxy; T = independently H, halo, OH, carboxy, carbamoyl, amino, cyano, NO2, alkenyl, alkynyl, cycloalkyl, (un)substituted alkyl, alkoxy; p = 0-5; L = aminocycloalkylideneamino, etc.; Y = bond, CH2, CO2, OCO, SO2, CO, CS, CONH, CSNH, etc.; with provisos; and pharmaceutically acceptable salts, hydrates, or solvates thereof] were prepared as antagonists of melanin concentrating hormone (MCH), an endogenous ligand of G-protein coupled receptors (GPCRs). Examples include solution and solid phase general synthetic methods and phys. data for nearly 3400 invention compds. In addition, all exemplified compds. were assayed using high throughput functional screening to detect intracellular Ca2+ concns. for accessing GPCR activation. For instance, reaction of 2,4-dichloro-6-methylpyrimidine with dimethylamine gave 2-chloro-4-(dimethylamino)-6-methylpyrimidine (40%), which was coupled with cis-(4-aminocyclohexyl)carbamic acid tert-Bu ester (60%). Deprotection (72%), amidation, and workup provided the benzamide IV•TFA. The latter demonstrated MCH antagonist activity with an IC50 value of 7.6 nM. Thus, pharmaceutical compns. comprising I are useful for the prophylaxis or treatment of improving memory function, sleeping and arousal, anxiety, depression, mood disorders, seizure, obesity, diabetes, appetite and eating disorders, cardiovascular disease, hypertension, dyslipidemia, myocardial infarction, binge eating disorders including bulimia, anorexia, mental disorders including manic depression, schizophrenia, delirium, dementia, stress, cognitive disorders, attention deficit disorder, substance abuse disorders, and dyskinesias including Parkinson's disease, epilepsy, and addiction (no data). This is part III of three in a series covering the patent.

IT **773140-54-8P**, N-[1-(4-Chlorophenyl)cyclopropyl]-N'-[cis-4-[[4-(dimethylamino)-5-methylpyrimidin-2-yl]amino]cyclohexyl]urea
773140-55-9P, N-[1-(4-Chlorophenyl)cyclopropyl]-N'-[cis-4-[[4-(dimethylamino)-6-methylpyrimidin-2-yl]amino]cyclohexyl]urea
773140-59-3P, N-[1-(4-Chlorophenyl)cyclopropyl]-N'-[cis-4-[[4-

(dimethylamino)-5-methylpyrimidin-2-yl]amino]cyclohexyl]-N-methylurea
773140-60-6P, N-[1-(4-Chlorophenyl)cyclopropyl]-N'-[cis-4-[[4-(dimethylamino)-6-methylpyrimidin-2-yl]amino]cyclohexyl]-N-methylurea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MCH antagonist; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

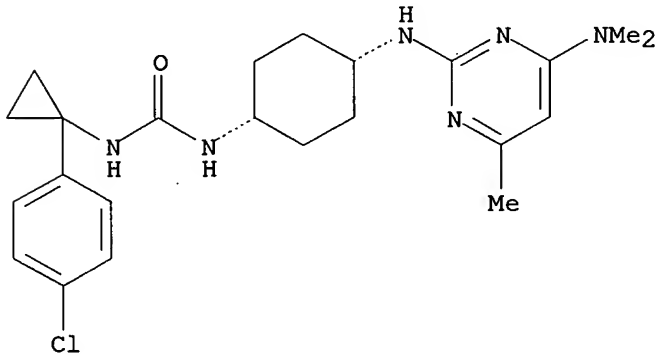
RN 773140-54-8 CAPLUS
CN Urea, N-[1-(4-chlorophenyl)cyclopropyl]-N'-[cis-4-[[4-(dimethylamino)-5-methyl-2-pyrimidinyl]amino]cyclohexyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



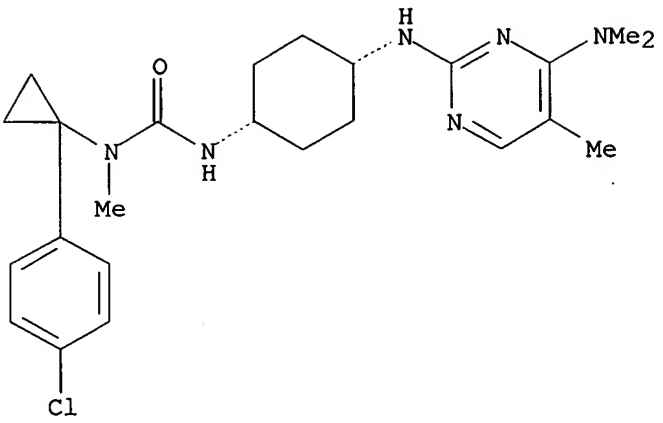
RN 773140-55-9 CAPLUS
CN Urea, N-[1-(4-chlorophenyl)cyclopropyl]-N'-[cis-4-[[4-(dimethylamino)-6-methyl-2-pyrimidinyl]amino]cyclohexyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



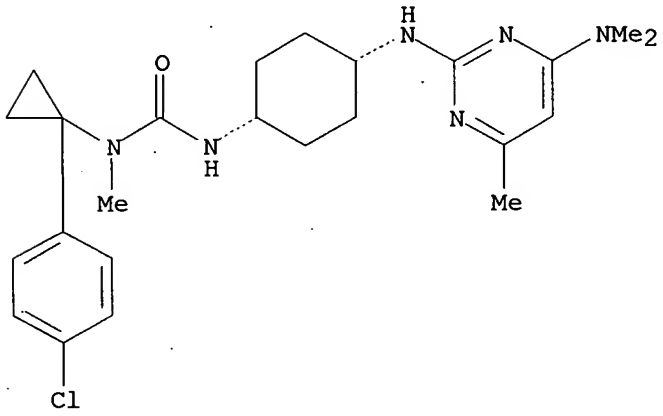
RN 773140-59-3 CAPLUS
CN Urea, N-[1-(4-chlorophenyl)cyclopropyl]-N'-[cis-4-[[4-(dimethylamino)-5-methyl-2-pyrimidinyl]amino]cyclohexyl]-N-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 773140-60-6 CAPLUS
CN Urea, N-[1-(4-chlorophenyl)cyclopropyl]-N'-[cis-4-[[4-(dimethylamino)-6-methyl-2-pyrimidinyl]amino]cyclohexyl]-N-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.



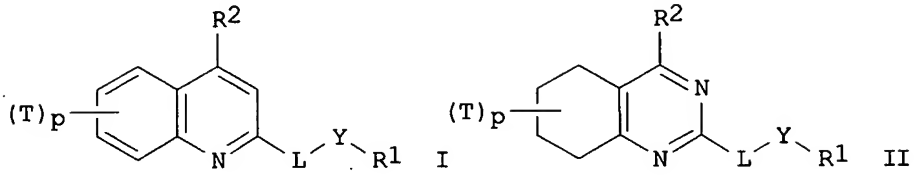
L3 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:875032 CAPLUS
DN 141:350191
TI Preparation of quinoline, tetrahydroquinazoline, and pyrimidine derivatives as MCH antagonist for treatment of CNS disorders
IN Sekiguchi, Yoshinori; Kanuma, Kosuke; Omodera, Katsunori; Busujima, Tsuyoshi; Tran, Thuy-Anh; Han, Sangdon; Casper, Martin; Kramer, Bryan A.; Semple, Graeme; Zou, Ning
PA Taisho Pharmaceutical Co. Ltd., Japan
SO Eur. Pat. Appl., 586 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

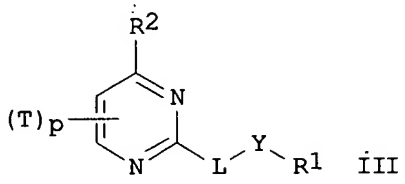
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1464335	A2	20041006	EP 2004-7651	20040330
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
	EP 1464335	A2	20041006	EP 2004-7651	20040330
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

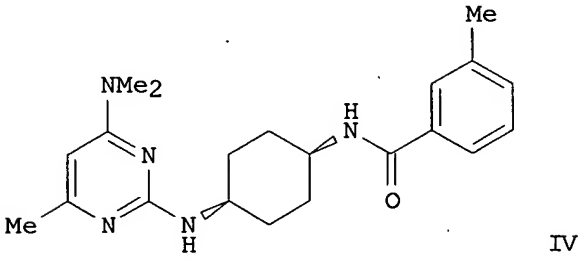
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

PRAI US 2003-458530P P 20030331
US 2003-495911P P 20030819
US 2003-510186P P 20031009
US 2003-530360P P 20031216
EP 2004-7651 A 20040330

GI







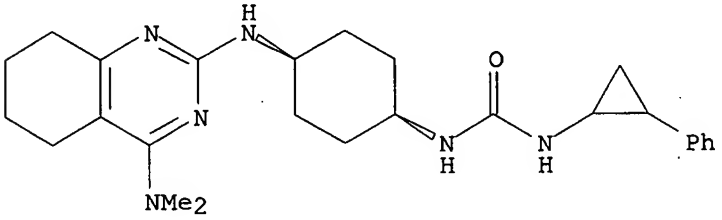
AB Title compds. I, II, and III [wherein R1 = (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl; R2 = H, halo, OH, carboxy, carbamoyl, amino, (un)substituted alkyl, alkoxy; T = independently H, halo, OH, carboxy, carbamoyl, amino, cyano, NO2, alkenyl, alkynyl, cycloalkyl, (un)substituted alkyl, alkoxy; p = 0-5; L = aminocycloalkylideneamino, etc.; Y = bond, CH2, CO2, OCO, SO2, CO, CS, CONH, CSNH, etc.; with provisos; and pharmaceutically acceptable salts, hydrates, or solvates thereof] were prepared as antagonists of melanin concentrating hormone (MCH), an endogenous ligand of G-protein coupled receptors (GPCRs). Examples include solution and solid phase general synthetic methods and phys. data for nearly 3400 invention compds. In addition, all exemplified compds. were assayed using high throughput functional screening to detect intracellular Ca2+ concns. for accessing GPCR activation. For instance, reaction of 2,4-dichloro-6-methylpyrimidine with dimethylamine gave 2-chloro-4-(dimethylamino)-6-methylpyrimidine (40%), which was coupled with cis-(4-aminocyclohexyl)carbamic acid tert-Bu ester (60%). Deprotection (72%), amidation, and workup provided the benzamide IV•TFA. The latter demonstrated MCH antagonist activity with an IC50 value of 7.6 nM. Thus, pharmaceutical compns. comprising I are useful for the prophylaxis or treatment of improving memory function, sleeping and arousal, anxiety, depression, mood disorders, seizure, obesity, diabetes, appetite and eating disorders, cardiovascular disease, hypertension,

dyslipidemia, myocardial infarction, binge eating disorders including bulimia, anorexia, mental disorders including manic depression, schizophrenia, delirium, dementia, stress, cognitive disorders, attention deficit disorder, substance abuse disorders, and dyskinesias including Parkinson's disease, epilepsy, and addiction (no data). This is part II of three in a series covering the patent.

IT **771535-28-5P 771539-54-9P 771540-43-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MCH antagonist; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

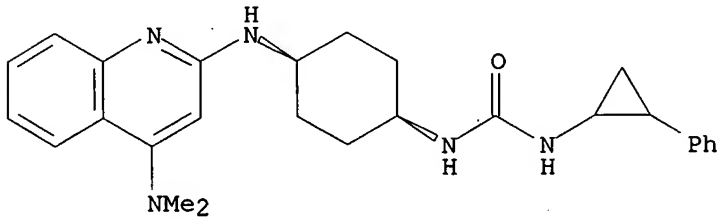
RN 771535-28-5 CAPLUS
CN Urea, N-[cis-4-[[4-(dimethylamino)-5,6,7,8-tetrahydro-2-quinazolinyl]amino]cyclohexyl]-N'-(2-phenylcyclopropyl)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 771539-54-9 CAPLUS
CN Urea, N-[cis-4-[[4-(dimethylamino)-2-quinolinyl]amino]cyclohexyl]-N'-(2-phenylcyclopropyl)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 771540-43-3 CAPLUS
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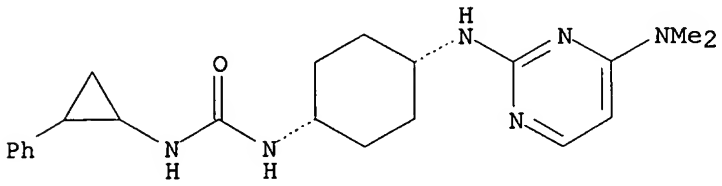
Relative stereochemistry.



L3 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:857578 CAPLUS

DN 141:350189
TI Preparation of novel quinazolines as MCH receptor antagonists
IN Sekiguchi, Yoshinori; Kanuma, Kosuke; Omodera, Katsunori; Busujima, Tsuyoshi; Tran, Thuy-Anh; Han, Sangdon; Casper, Martin; Kramer, Bryan A.
PA Taisho Pharmaceutical Co., Ltd., Japan; Arena Pharmaceuticals Inc.
SO PCT Int. Appl., 363 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004087680	A1	20041014	WO 2004-JP4554	20040330

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-458424P P 20030331
OS MARPAT 141:350189
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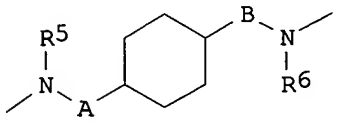

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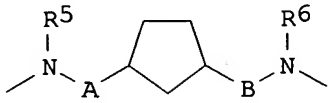


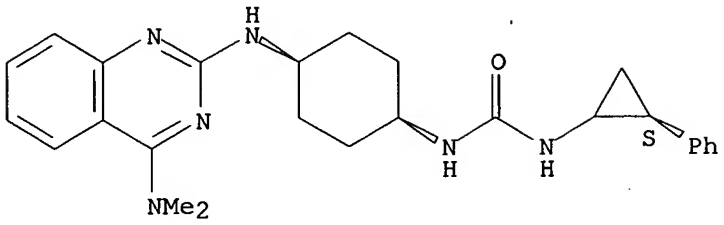
II

AB The title compds. QLYR1 [I; Q = (un)substituted 2-quinazolinyl; R1 = (un)substituted alkyl, cycloalkyl, aryl, etc.; L = II, III (wherein R5, R6 = H, alkyl; A, B = a bond, CH2, (CH2)2), etc.; Y = (un)substituted CONH, CSNH, C(O)O, SO2, etc.] which act as MCH receptor antagonists, were prepared E.g., a multi-step synthesis of 1-(3,4-dimethoxyphenyl)-3-[cis-4-(4-dimethylaminoquinazolin-2-ylamino)cyclohexyl]-urea hydrochloride (starting from quinazoline-2,4-dione) which showed IC50 of 13 nM against MCH receptor binding, was given. The compds. I are useful in pharmaceutical compns. (claimed) which use includes prophylaxis or treatment of improving memory function, sleeping and arousal, anxiety, depression, mood disorders, seizure, obesity, diabetes, appetite and eating disorders, cardiovascular disease, hypertension, dyslipidemia, myocardial infarction, binge eating disorders including bulimia, anorexia, mental disorders including manic depression, schizophrenia, delirium, dementia, stress, cognitive disorders, attention deficit disorder, substance abuse disorders and dyskinesias including Parkinson's disease, epilepsy, and addiction.

IT **774199-67-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel quinazolines as MCH receptor antagonists)

RN 774199-67-6 CAPLUS
CN Urea, N-[cis-4-[[4-(dimethylamino)-2-quinazolinyl]amino]cyclohexyl]-N'-[(2S)-2-phenylcyclopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:622568 CAPLUS
DN 139:164710
TI Preparation of ureidoalkylpiperidines as modulators of chemokine CCR3 receptor activity.
IN Ko, Soo S.; Delucca, George V.; Duncia, John V.; Santella, Joseph B., III; Wacker, Dean A.
PA Bristol-Myers Squibb Pharma Company, USA
SO U.S., 145 pp., Cont.-in-part of U.S. Ser. No. 465,286, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6605623	B1	20030812	US 2000-598821	20000621
	US 6331541	B1	20011218	US 1999-465288	19991217
	ZA 2001003756	A	20020509	ZA 2001-3756	20010509
	CA 2413274	AA	20011227	CA 2001-2413274	20010620
	WO 2001098269	A2	20011227	WO 2001-US19745	20010620
	WO 2001098269	A3	20030710		
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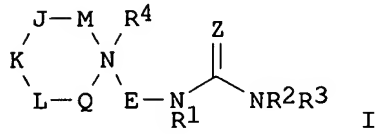
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1363881	A2	20031126	EP 2001-950358	20010620
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	JP 2004517803	T2	20040617	JP 2002-504225	20010620
	US 2003013741	A1	20030116	US 2001-7172	20011023
	US 6521592	B2	20030218		
	US 2004002515	A1	20040101	US 2002-279416	20021024
	US 6875776	B2	20050405		
	US 2004006107	A1	20040108	US 2002-279231	20021024
	US 6780857	B2	20040824		
	US 2004058960	A1	20040325	US 2003-465191	20030619
	US 6906066	B2	20050614		
PRAI	US 1998-112717P	P	19981218		
	US 1999-161243P	P	19991022		
	US 1999-465286	B2	19991217		
	US 1999-161137P	P	19991022		

	US 1999-161184P	P	19991022
	US 1999-161222P	P	19991022
	US 1999-465287	A3	19991217
	US 1999-465288	A3	19991217
	US 1999-465948	A3	19991217
	US 2000-213051P	P	20000621
	US 2000-598821	A	20000621
	WO 2001-US19745	W	20010620

OS MARPAT 139:164710

GI



I

AB [Title compds. I; M = CH2, CHR5, CHR13, CR13R13, CR5R13; Q = CH2, CHR5, CHR13, CR13R13, CR5R13; J, L = CH2, CHR5, CHR6, CR6R6, CR5R6; Z = O, S; M = CH2, CHR5, CHR13, CR13R13, CR5R13; K = CHR5, CR5R6; Z = O, S; E = (CHR7)(CHR9)v(CR11R12); R1, R2 = H, alkyl, alkenyl, alkynyl, (substituted) alkylcycloalkyl; R2R3 = atoms to form a (substituted) 5-7 membered ring; R3, R5 = (substituted) (alkyl)cycloalkyl, (alkyl)heterocyclyl; R4 = null, O, alkyl, alkenyl, alkynyl, etc.; R4 with R7, R9, or R11 = atoms to form a 5-7 membered ring; R6 = alkyl, alkenyl, alkynyl, etc.; R7, R9 = H; R4R7, R4R9 = (substituted) spirocyclyl; R13 = alkyl, alkenyl, alkynyl, cycloalkyl, etc.; R11R12 = pyrrolidinyl, tetrahydrofuryl, piperidinyl, tetrahydropyranyl; v = 1, 2], were prepared as modulators of chemokine activity (no data) for preventing asthma and other allergic diseases. Thus, 4-benzyl-1-(3-aminopropyl)piperidine (preparation given) in THF was treated with 3-cyanophenyl isocyanate to give N-(3-cyanophenyl)-N'-[3-[4-(phenylmethyl)-1-piperidinyl]propyl]urea. A pharmaceutical composition comprising the compound I was claimed.

IT **275812-98-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of ureidoalkylpiperidines as modulators of chemokine CCR3 receptor activity)

RN 275812-98-1 CAPLUS

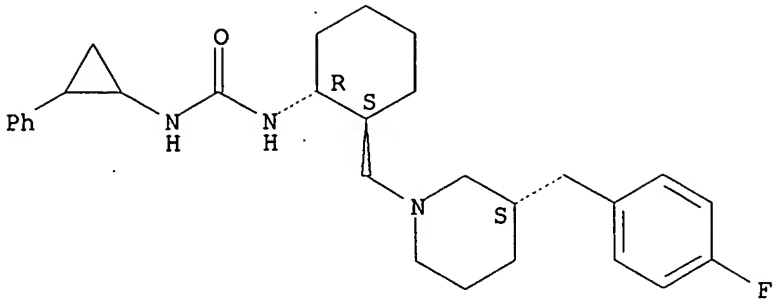
CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 275812-97-0

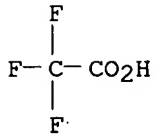
CMF C29 H38 F N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:150534 CAPLUS
DN 138:204946
TI Preparation of N-ureidoalkylpiperidines as modulators of CCR3 chemokine receptor activity for the prevention of asthma and other allergic diseases
IN Ko, Soo S.; Delucca, George V.; Duncia, John V.; Kim, Ui Tae; Wacker, Dean A.; Zheng, Changsheng
PA Bristol-Myers Squibb Pharma Company, USA
SO U.S., 126 pp., Cont.-in-part of U.S. Ser. No. 466,442.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 10

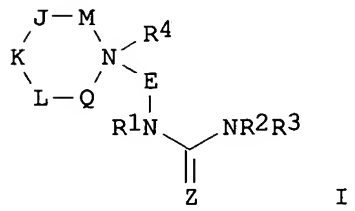
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6525069	B1	20030225	US 2000-597400	20000621
US 6331541	B1	20011218	US 1999-465288	19991217
US 6444686	B1	20020903	US 1999-466442	19991217
ZA 2001003756	A	20020509	ZA 2001-3756	20010509
CA 2413421	AA	20011227	CA 2001-2413421	20010620
WO 2001098270	A2	20011227	WO 2001-US19752	20010620
WO 2001098270	A3	20020530		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1294690	A2	20030326	EP 2001-950360	20010620

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

	JP 2004516238	T2	20040603	JP 2002-504226	20010620
	US 2003013741	A1	20030116	US 2001-7172	20011023
	US 6521592	B2	20030218		
	US 2003114489	A1	20030619	US 2002-180869	20020626
	US 6897234	B2	20050524		
	US 2004002515	A1	20040101	US 2002-279416	20021024
	US 6875776	B2	20050405		
	US 2004006107	A1	20040108	US 2002-279231	20021024
	US 6780857	B2	20040824		
	US 2004034063	A1	20040219	US 2003-359443	20030206
	US 2005096325	A1	20050505	US 2004-983367	20041108
PRAI	US 1998-112717P	P	19981218		
	US 1999-161221P	P	19991022		
	US 1999-466442	A2	19991217		
	US 1999-161137P	P	19991022		
	US 1999-161184P	P	19991022		
	US 1999-161222P	P	19991022		
	US 1999-465287	A3	19991217		
	US 1999-465288	A3	19991217		
	US 1999-465948	A3	19991217		
	US 2000-213208P	P	20000621		
	US 2000-597400	A	20000621		
	WO 2001-US19752	W	20010620		
	US 2002-180869	A1	20020626		

OS MARPAT 138:204946

GI



I

AB Title compds. [I; M, Q = CH2, CHR5, CHR13, CR13R13, CR5R13; J, K, L = CH2, CHR5, CHR6, CR6R6, CR5R6; ≥1 of J, K, L contains R5; Z = O, S, NR1a, CHCN, CHNO2, C(CN)2; R1a = H, alkyl, cycloalkyl, CN, NO2, etc.; E = (substituted) C3-6 carbocyclyl, methylenecarbocyclyl, ethylenecarbocyclyl, etc.; R1, R2 = H, alkyl, alkenyl, alkynyl; R3 = (substituted) alkyl, alkenyl, alkynyl; R4 = null, N-oxide, alkyl, alkenyl, alkynyl, cycloalkylalkyl, etc.; R5 = (substituted) alkylenecarbocyclyl, alkyleneheterocyclyl; R6 = alkyl, alkenyl, alkynyl, alkylcycloalkyl, perfluoroalkyl, hydroxyalkyl, mercaptoalkyl, aminoalkyl, CN, etc.; R13 = alkyl, alkenyl, alkynyl, cycloalkyl, perfluoroalkyl, aminoalkyl, hydroxyalkyl, carboxyalkyl, mercaptoalkyl, acylaminoalkyl, (substituted) phenylalkyl, etc.], were prepared as CCR3 modulators (no data). Thus, 4-benzyl-1-(3-aminopropyl)piperidine (preparation given) and 3-cyanophenyl isocyanate were stirred 30 min. in THF to give N-3-cyanophenyl-N'-[3-[4-(phenylmethyl)-1-piperidinyl]propyl]urea.

IT **275812-98-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-ureidoalkylpiperidines as modulators of chemokine receptor activity)

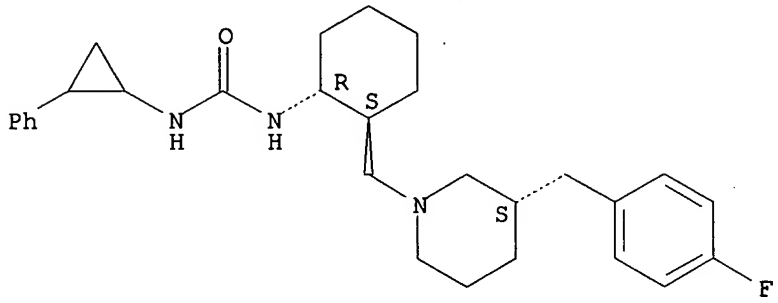
RN 275812-98-1 CAPLUS

CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

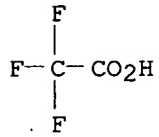
CRN 275812-97-0
CMF C29 H38 F N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:935575 CAPLUS
DN 136:69739
TI Preparation of piperidinoalkylureas as chemokine receptor modulators
IN Ko, Soo S.; Delucca, George V.; Duncia, John V.; Kim, Ui Tae; Wacker, Dean A.; Zheng, Changsheng
PA Dupont Pharmaceuticals Company, USA
SO PCT Int. Appl., 333 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001098270	A2	20011227	WO 2001-US19752	20010620
	WO 2001098270	A3	20020530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,

ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6525069	B1	20030225	US 2000-597400	20000621
CA 2413421	AA	20011227	CA 2001-2413421	20010620
EP 1294690	A2	20030326	EP 2001-950360	20010620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004516238	T2	20040603	JP 2002-504226	20010620
PRAI US 2000-213208P	P	20000621		
US 2000-597400	A	20000621		
US 1998-112717P	P	19981218		
US 1999-161221P	P	19991022		
US 1999-466442	A2	19991217		
WO 2001-US19752	W	20010620		

OS MARPAT 136:69739

AB The title compds. were prepared as chemokine receptor modulators (no data). Thus, PhCH2Z(CH2)3NHR (Z = piperidine-4,1-diyl)(I; R = H)(preparation given) was amidated by 3-(NC)C6H4NCO to give I [R = CONHC6H4(CN)-3].

IT **275812-98-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinoalkylureas as chemokine receptor modulators)

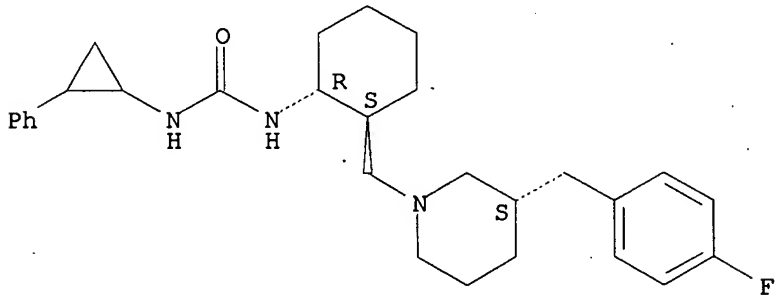
RN 275812-98-1 CAPLUS

CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

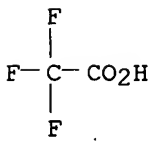
CRN 275812-97-0
CMF C29 H38 F N3 O

Absolute stereochemistry.



CM 2

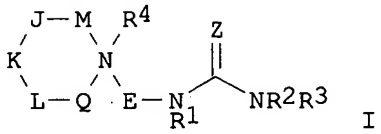
CRN 76-05-1
CMF C2 H F3 O2



L3 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:935574 CAPLUS
DN 136:69738
TI Preparation of ureidoalkylpiperidines as modulators of chemokine CCR3 receptor activity.
IN Ko, Soo S.; Delucca, George V.; Duncia, John V.; Santella, Joseph B.; Wacker, Dean A.; Yao, Wenqing
PA Dupont Pharmaceuticals Company, USA; Bristol-Myers Squibb Pharmaceutical Co.
SO PCT Int. Appl., 446 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001098269	A2	20011227	WO 2001-US19745	20010620
	WO 2001098269	A3	20030710		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6605623	B1	20030812	US 2000-598821	20000621
	CA 2413274	AA	20011227	CA 2001-2413274	20010620
	EP 1363881	A2	20031126	EP 2001-950358	20010620
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	JP 2004517803	T2	20040617	JP 2002-504225	20010620
PRAI	US 2000-213051P	P	20000621		
	US 2000-598821	A	20000621		
	US 1998-112717P	P	19981218		
	US 1999-161243P	P	19991022		
	US 1999-465286	B2	19991217		
	WO 2001-US19745	W	20010620		

OS MARPAT 136:69738
GI



I

AB [Title compds. I; M = CH2, CHR5, CHR13, CR13R13, CR5R13; Q = CH2, CHR5, CHR13, CR13R13, CR5R13; J, L = CH2, CHR5, CHR6, CR6R6, CR5R6; Z = O, S; M = CH2, CHR5, CHR13, CR13R13, CR5R13; K = CHR5, CR5R6; Z = O, S; E = (CHR7)(CHR9)v(CR11R12); R1, R2 = H, alkyl, alkenyl, alkynyl, (substituted) alkylcycloalkyl; R2R3 = atoms to form a (substituted) 5-7 membered ring; R3, R5 = (substituted) (alkyl)cycloalkyl, (alkyl)heterocyclyl; R4 = null, O, alkyl, alkenyl, alkynyl, etc.; R4 with R7, R9, or R11 = atoms to form a

5-7 membered ring; R7, R9 = H; R4R7, R4R9 = (substituted) spirocyclyl; R13 = alkyl, alkenyl, alkynyl, cycloalkyl, etc.; R11R12 = pyrrolidinyl, tetrahydrofuryl, piperidinyl, tetrahydropyranyl; v = 1, 2], were prepared as modulators of chemokine activity (no data). Thus, 4-benzyl-1-(3-aminopropyl)piperidine (preparation given) in THF was treated with 3-cyanophenyl isocyanate to give N-(3-cyanophenyl)-N'-[3-[4-(phenylmethyl)-1-piperidinyl]propyl]urea.

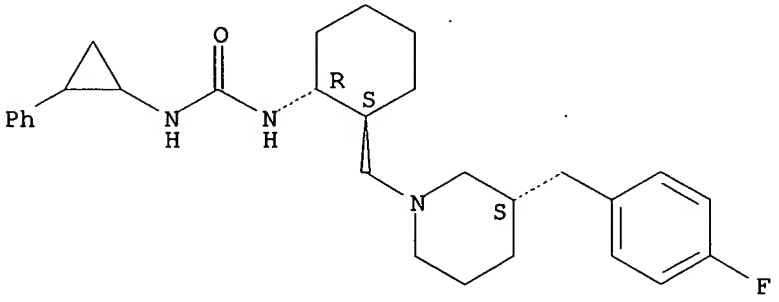
IT **275812-98-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ureidoalkylpiperidines as modulators of chemokine CCR3 receptor activity)

RN 275812-98-1 CAPLUS
CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

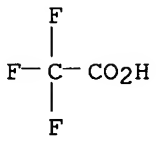
CRN 275812-97-0
CMF C29 H38 F N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

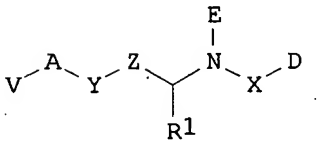


L3 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:824211 CAPLUS
DN 134:4764
TI Preparation of 3-(benzoylamino)propionic acid derivatives as glucagon antagonists/inverse agonists
IN Ling, Anthony; Plewe, Michael Bruno; Truesdale, Larry Kenneth; Lau, Jesper; Madsen, Peter; Sams, Christian; Behrens, Carsten; Vagner, Josef; Christensen, Inge Thoger; Lundt, Behrend Frederik; Sidelmann, Ulla Grove; Thogersen, Henning

PA Novo Nordisk A/S, Den.; Agouron Pharmaceuticals, Inc.
SO PCT Int. Appl., 564 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000069810	A1	20001123	WO 2000-DK264	20000516
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6503949	B1	20000516	US 2000-572553	20000516
	CA 2373892	AA	20001123	CA 2000-2373892	20000516
	EP 1183229	A1	20020306	EP 2000-926725	20000516
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 2000010651	A	20020319	BR 2000-10651	20000516
	JP 2002544254	T2	20021224	JP 2000-618228	20000516
	ZA 2001008560	A	20020613	ZA 2001-8560	20011018
	NO 2001005607	A	20020117	NO 2001-5607	20011116
	US 2003220350	A1	20031127	US 2002-233851	20020830
	US 6875760	B2	20050405		
PRAI	DK 1999-684	A	19990517		
	DK 2000-478	A	20000321		
	US 1999-134415P	P	19990517		
	US 2000-191685P	P	20000323		
	US 2000-572553	A3	20000516		
	WO 2000-DK264	W	20000516		

OS MARPAT 134:4764
GI



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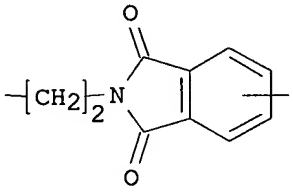
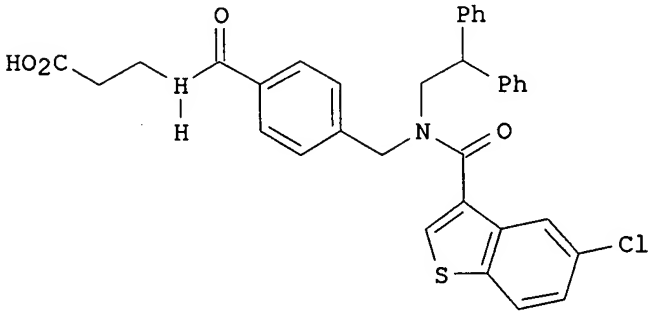


II



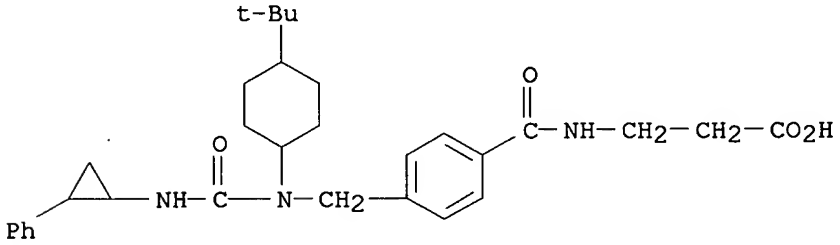
III

AB The title compds. [I; V = CO2R2, CONR2R3, CONR2OR3, etc. (wherein R2, R3 = H, alkyl); A = (CH2)n(CR8R9)bNR7, (CR8R9)b(CH2)nNR7, (CR8R9)b(CH2)n, etc. (b = 0-1; n = 0-3; R7 = H, alkyl, (cycloalkyl)alkyl; R8, R9 = H, alkyl); Y = CO, SO2, O, a bond; Z = (un)substituted phenylene, divalent radical derived from 5-6 membered heteroarom. ring containing 1-2 heteroatoms selected from N, O and S; or AYZ together = II; R1 = H, alkyl; X = CO(CR13R14)r(CH2)s, SO2(CR13R14)r(CH2)s, CO2(CR13R14)r(CH2)s, etc. (r = 0-1; s = 0-3; R13, R14 = H, alkyl); D = (un)substituted Ph, pyridyl, cyclopropyl, etc.; E = (un)substituted quinolinyl, 2,5-dioxopiperidinyl, biphenylalkyl, etc.] which act to antagonize the action of the glucagon hormone on the glucagon receptor (data given), and therefore may be suitable for the treatment and/or prevention of any glucagon-mediated conditions and diseases such as hyperglycemia, Type 1 diabetes, Type 2 diabetes and obesity, were prepared and formulated. E.g., a multi-step solid phase synthesis of III was given. Compds. I are effective at 0.05-10 mg/kg/day.

IT **307983-80-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 3-(benzoylamino)propionic acid derivs. as glucagon antagonists/inverse agonists)

RN 307983-80-8 CAPLUS

CN β-Alanine, N-[4-[[[4-(1,1-dimethylethyl)cyclohexyl][[(2-phenylcyclopropyl)amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



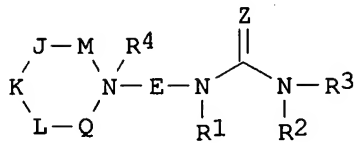
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:420964 CAPLUS
DN 133:43445
TI Preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity
IN Ko, Soo S.; Duncia, John V. K.; Santella, Joseph B., III; Wacker, Dean A.; Kim, Ui Tae
PA Du Pont Pharmaceuticals Company, USA
SO PCT Int. Appl., 351 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000035454	A1	20000622	WO 1999-US30336	19991217

W: AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
CA 2348923 AA 20000622 CA 1999-2348923 19991217
EP 1140087 A1 20011010 EP 1999-965322 19991217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
US 6331541 B1 20011218 US 1999-465288 19991217
US 6492400 B1 20021210 US 1999-465287 19991217
ZA 2001003756 A 20020509 ZA 2001-3756 20010509
US 2003013741 A1 20030116 US 2001-7172 20011023
US 6521592 B2 20030218
US 2004002515 A1 20040101 US 2002-279416 20021024
US 6875776 B2 20050405
US 2004006107 A1 20040108 US 2002-279231 20021024
US 6780857 B2 20040824
PRAI US 1998-112717P P 19981218
US 1999-161184P P 19991022
US 1999-161137P P 19991022
US 1999-161222P P 19991022
US 1999-465287 A3 19991217
US 1999-465288 A3 19991217
US 1999-465948 A3 19991217
WO 1999-US30336 W 19991217
OS MARPAT 133:43445
GI



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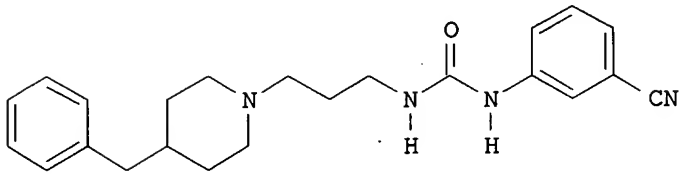


II

AB The title compds. [I; M = absent, CH2, CH(CH2Ph), etc,; Q = CH2, CHR5, etc.; J, K, L = CH2, CH(CH2Ph), etc.; Z = O, S; E = (CH2)2, (CH2)3, CH2CH(OH)CH(Ph), etc.; R1, R2 = H, alkyl, alkenyl, etc.; R2 and R3 may join to form (un)substituted 5-7 membered ring; R3 = (un)substituted Ph, naphthyl, adamantyl, etc.; R4 = absent, alkyl, alkenyl, etc.], modulators of CCR3 useful for the prevention of asthma and other allergic diseases, were prepared and formulated. E.g., a multi-step synthesis of II was given. Compds. I are effective at 1.0-20 mg/kg/da (oral dosage).

IT **275812-98-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity)

RN 275812-98-1 CAPLUS

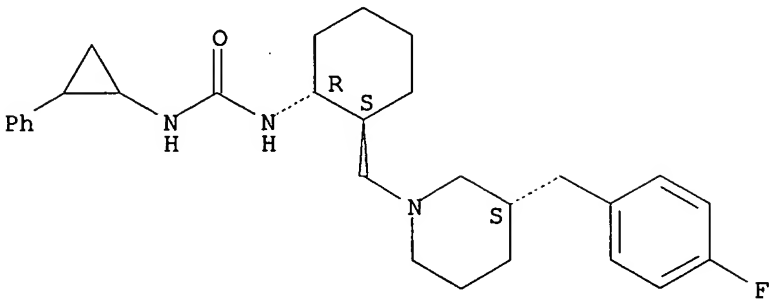
CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)-,

mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

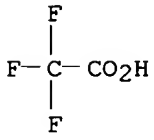
CRN 275812-97-0
CMF C29 H38 F N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:420963 CAPLUS
DN 133:43444
TI Preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity
IN Ko, Soo; Clark, Cheryl Mcardle; Delucca, George V.; Duncia, John V.; Santella, Joseph B., III; Wacker, Dean A.
PA Du Pont Pharmaceuticals Co., USA
SO PCT Int. Appl., 316 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

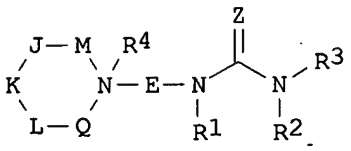
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000035453	A1	20000622	WO 1999-US30335	19991217
W: AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2347909	AA	20000622	CA 1999-2347909	19991217
EP 1158980	A1	20011205	EP 1999-965321	19991217

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

	US 6331541	B1	20011218	US 1999-465288	19991217
	US 6486180	B1	20021126	US 1999-465948	19991217
	ZA 2001003756	A	20020509	ZA 2001-3756	20010509
	US 2003013741	A1	20030116	US 2001-7172	20011023
	US 6521592	B2	20030218		
	US 2004002515	A1	20040101	US 2002-279416	20021024
	US 6875776	B2	20050405		
	US 2004006107	A1	20040108	US 2002-279231	20021024
	US 6780857	B2	20040824		
PRAI	US 1998-112717P	P	19981218		
	US 1999-161137P	P	19991022		
	US 1999-161184P	P	19991022		
	US 1999-161222P	P	19991022		
	US 1999-465287	A3	19991217		
	US 1999-465288	A3	19991217		
	US 1999-465948	A3	19991217		
	WO 1999-US30335	W	19991217		

OS MARPAT 133:43444

GI



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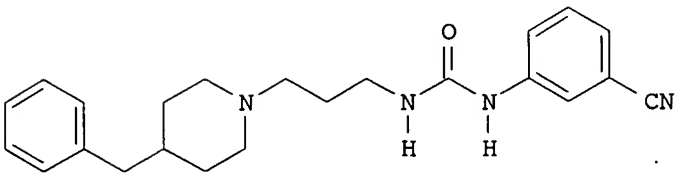


II

AB The title compds. [I; M = absent, CH2, CH(CH2Ph), etc,; Q = CH2, CH(CH2Ph), etc.; J, K, L = CH2, CH(CH2Ph), etc.; Z = O, S; E = (CH2)2, (CH2)3, CH2CH(OH)CH(Ph), etc.; R1, R2 = H, alkyl, alkenyl, etc.; R2 and R3 may join to form (un)substituted 5-7 membered ring; R3 = (un)substituted Ph, naphthyl, adamantyl, etc.; R4 = absent, alkyl, alkenyl, etc.], modulators of CCR3 useful for the prevention of asthma and other allergic diseases, were prepared and formulated. E.g., a multi-step synthesis of II was given. Compds. I are effective at 1.0-20 mg/kg/day (oral dosage).

IT **275812-98-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity)

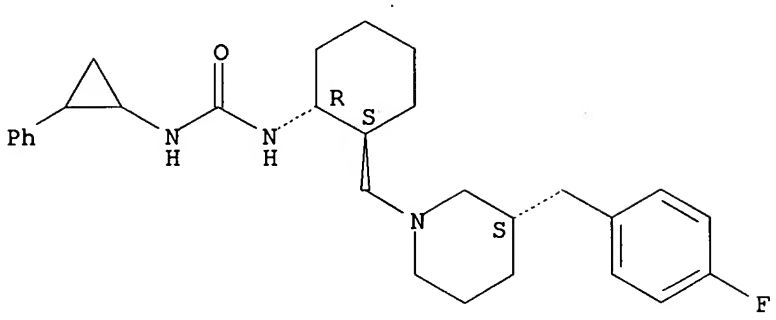
RN 275812-98-1 CAPLUS

CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

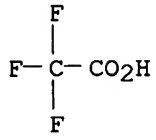
CRN 275812-97-0
CMF C29 H38 F N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

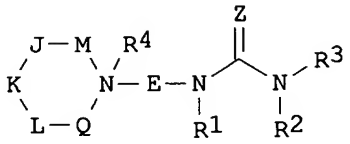
L3 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:420962 CAPLUS
DN 133:43443
TI Preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity
IN Ko, Soo S.; Delucca, George V.; Duncia, John V.; Kim, Ui Tae; Santella, Joseph B. Iii; Wacker, Dean A. K.
PA Du Pont Pharmaceuticals Company, USA
SO PCT Int. Appl., 388 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000035452	A1	20000622	WO 1999-US30334	19991217
	W: AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2347770	AA	20000622	CA 1999-2347770	19991217
	EP 1161240	A1	20011212	EP 1999-963107	19991217
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6331541	B1	20011218	US 1999-465288	19991217
	TR 200101859	T2	20011221	TR 2001-200101859	19991217

	BR 9917038	A	20020402	BR 1999-17038	19991217
	JP 2002532427	T2	20021002	JP 2000-587772	19991217
	NZ 511394	A	20030725	NZ 1999-511394	19991217
	AU 770042	B2	20040212	AU 2000-19406	19991217
	ZA 2001003756	A	20020509	ZA 2001-3756	20010509
	NO 2001002977	A	20010820	NO 2001-2977	20010615
	US 2003013741	A1	20030116	US 2001-7172	20011023
	US 6521592	B2	20030218		
	US 2004002515	A1	20040101	US 2002-279416	20021024
	US 6875776	B2	20050405		
	US 2004006107	A1	20040108	US 2002-279231	20021024
	US 6780857	B2	20040824		
	US 2005096325	A1	20050505	US 2004-983367	20041108
PRAI	US 1998-112717P	P	19981218		
	US 1999-161221P	P	19991022		
	US 1999-161137P	P	19991022		
	US 1999-161184P	P	19991022		
	US 1999-161222P	P	19991022		
	US 1999-465287	A3	19991217		
	US 1999-465288	A3	19991217		
	US 1999-465948	A3	19991217		
	US 1999-466442	A3	19991217		
	WO 1999-US30334	W	19991217		
	US 2002-180869	A1	20020626		

OS MARPAT 133:43443

GI



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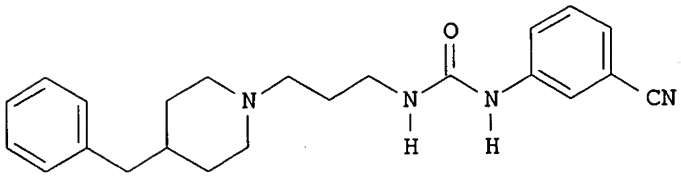


II

AB The title compds. [I; M = absent, CH2, CH(CH2Ph), etc,; Q = CH2, CH(CH2Ph), etc.; J, K, L = CH2, CH(CH2Ph), etc.; Z = O, S; E = (CH2)2, (CH2)3, CH2CH(OH)CH(Ph), etc.; R1, R2 = H, alkyl, alkenyl, etc.; R2 and R3 may join to form (un)substituted 5-7 membered ring; R3 = (un)substituted Ph, naphthyl, adamantyl, etc.; R4 = absent, alkyl, alkenyl, etc.], modulators of CCR3 useful for the prevention of asthma and other allergic diseases, were prepared and formulated. E.g., a multi-step synthesis of II was given. Compds. I are effective at 1.0-20 mg/kg/day (oral dosage).

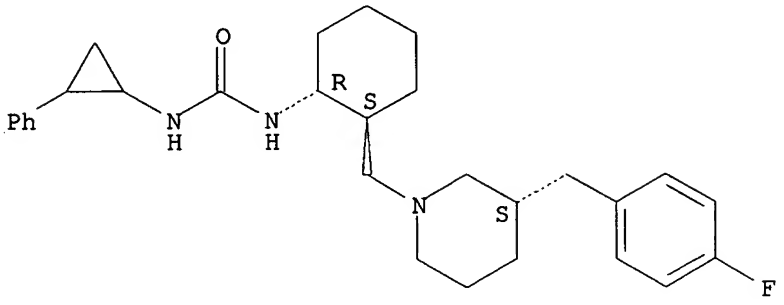
IT **275812-97-0P 275812-98-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity)

RN 275812-97-0 CAPLUS

CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-

piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

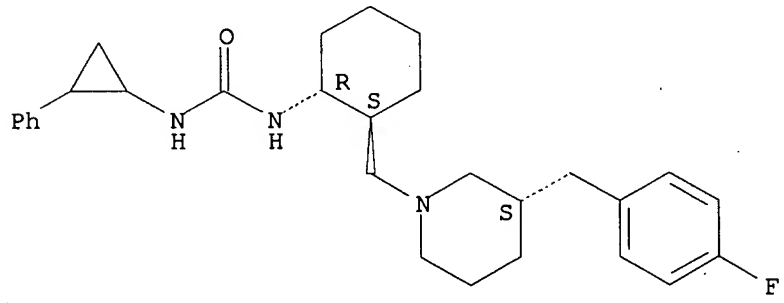


RN 275812-98-1 CAPLUS
CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

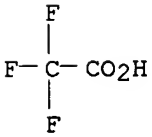
CRN 275812-97-0
CMF C29 H38 F N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



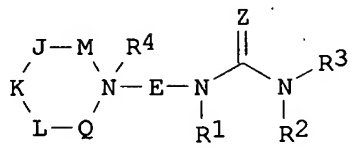
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:420961 CAPLUS

DN 133:43442
TI Preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity
IN Ko, Soo S.; Delucca, George V.; Duncia, John V.; Santella, Joseph B., III; Wacker, Dean A.; Watson, Paul S.; Varnes, Jeffrey G.
PA Du Pont Pharmaceuticals Company, USA
SO PCT Int. Appl., 394 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000035451	A1	20000622	WO 1999-US30332	19991217
	W: AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2350730	AA	20000622	CA 1999-2350730	19991217
	EP 1140086	A1	20011010	EP 1999-964297	19991217
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6331541	B1	20011218	US 1999-465288	19991217
	ZA 2001003756	A	20020509	ZA 2001-3756	20010509
	US 2003013741	A1	20030116	US 2001-7172	20011023
	US 6521592	B2	20030218		
	US 2004002515	A1	20040101	US 2002-279416	20021024
	US 6875776	B2	20050405		
	US 2004006107	A1	20040108	US 2002-279231	20021024
	US 6780857	B2	20040824		
PRAI	US 1998-112717P	P	19981218		
	US 1999-161243P	P	19991022		
	US 1999-161137P	P	19991022		
	US 1999-161184P	P	19991022		
	US 1999-161222P	P	19991022		
	US 1999-465287	A3	19991217		
	US 1999-465288	A3	19991217		
	US 1999-465948	A3	19991217		
	WO 1999-US30332	W	19991217		

OS MARPAT 133:43442
GI



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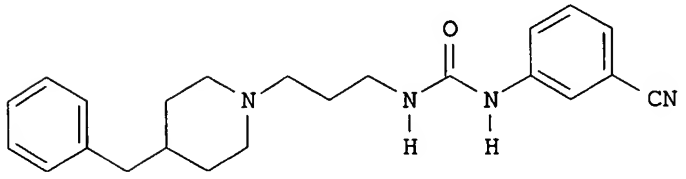


II

AB The title compds. [I; M = absent, CH2, CH(CH2Ph), etc,; Q = CH2, CH(CH2Ph), etc.; J, K, L = CH2, CH(CH2Ph), etc.; Z = O, S; E = (CH2)2, (CH2)3, CH2CH(OH)CH(Ph), etc.; R1, R2 = H, alkyl, alkenyl, etc.; R2 and R3 may join to form (un)substituted 5-7 membered ring; R3 = (un)substituted Ph, naphthyl, adamantyl, etc.; R4 = absent, alkyl, alkenyl, etc.], modulators of CCR3 useful for the prevention of asthma and other allergic diseases, were prepared and formulated. E.g., a multi-step synthesis of II was given. Compds. I are effective at 1.0-20 mg/kg/day (oral dosage).

IT **275812-98-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity)

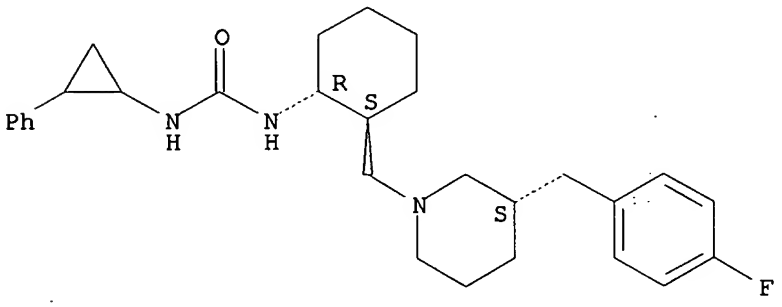
RN 275812-98-1 CAPLUS

CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

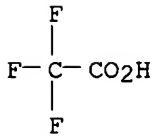
CRN 275812-97-0
CMF C29 H38 F N3 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:420959 CAPLUS
DN 133:43441
TI Preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity
IN Ko, Soo S.; Delucca, George V.; Duncia, John V.; Santella, Joseph B., III;

Gardner, Daniel S.
PA Du Pont Pharmaceuticals Company, USA
SO PCT Int. Appl., 327 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000035449	A1	20000622	WO 1999-US30292	19991217
	W: AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2346933	AA	20000622	CA 1999-2346933	19991217
	EP 1156807	A1	20011128	EP 1999-968144	19991217
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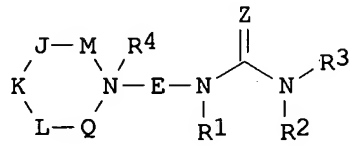
	US 6331541	B1	20011218	US 1999-465288	19991217
	TR 200101859	T2	20011221	TR 2001-200101859	19991217
	ZA 2001003756	A	20020509	ZA 2001-3756	20010509
	US 2003013741	A1	20030116	US 2001-7172	20011023
	US 6521592	B2	20030218		
	US 2004002515	A1	20040101	US 2002-279416	20021024
	US 6875776	B2	20050405		
	US 2004006107	A1	20040108	US 2002-279231	20021024
	US 6780857	B2	20040824		
	US 2005096325	A1	20050505	US 2004-983367	20041108
PRAI	US 1998-112717P	P	19981218		
	US 1999-161221P	P	19991022		
	US 1999-161122P	P	19991022		
	US 1999-161137P	P	19991022		
	US 1999-161184P	P	19991022		
	US 1999-161222P	P	19991022		
	US 1999-465287	A3	19991217		
	US 1999-465288	A3	19991217		
	US 1999-465948	A3	19991217		
	US 1999-466442	A3	19991217		
	WO 1999-US30292	W	19991217		
	US 2002-180869	A1	20020626		

OS MARPAT 133:43441
GI



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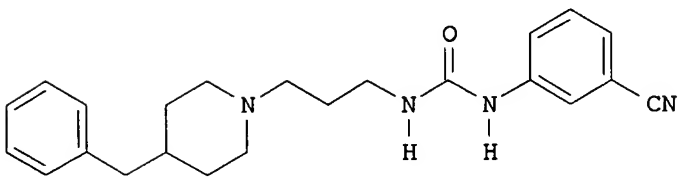


II

AB The title compds. [I; M = absent, CH2, CH(CH2Ph), etc,; Q = CH2, CHR5, etc.; J, K, L = CH2, CH(CH2Ph), etc.; Z = O, S; E = (CH2)2, (CH2)3, CH2CH(OH)CH(Ph), etc.; R1, R2 = H, alkyl, alkenyl, etc.; R2 and R3 may join to form (un)substituted 5-7 membered ring; R3 = (un)substituted Ph, naphthyl, adamantyl, etc.; R4 = absent, alkyl, alkenyl, etc.], modulators of CCR3 useful for the prevention of asthma and other allergic diseases, were prepared and formulated. E.g., a multi-step synthesis of II was given. Compds. I are effective at 1.0-20 mg/kg/day (oral dosage).

IT **275812-98-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-ureidoalkyl-piperidines as modulators of chemokine receptor activity)

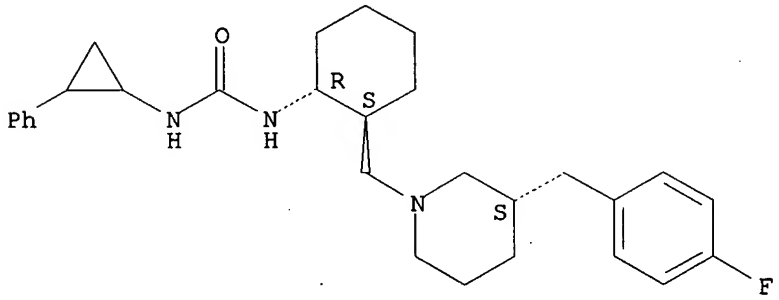
RN 275812-98-1 CAPLUS

CN Urea, N-[(1R,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]cyclohexyl]-N'-(2-phenylcyclopropyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

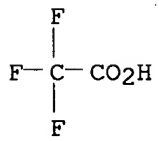
CRN 275812-97-0
CMF C29 H38 F N3 O

Absolute stereochemistry.



CM 2

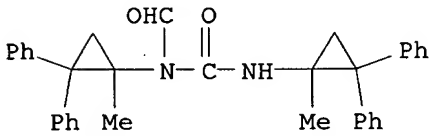
CRN 76-05-1
CMF C2 H F3 O2



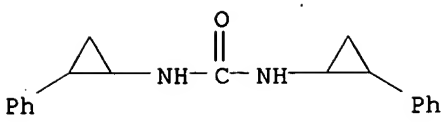
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1972:84961 CAPLUS
DN 76:84961
TI Synthesis of isonitriles
AU Walborsky, H. M.; Niznik, G. E.

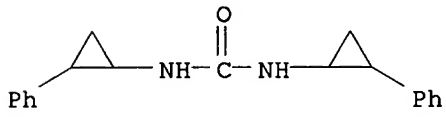
CS Dep. Chem., Florida State Univ., Tallahassee, FL, USA
SO Journal of Organic Chemistry (1972), 37(2), 187-90
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
OS CASREACT 76:84961
AB A synthesis of iso-nitriles was devised using a DMF solution of chlorodimethylfor-miminium chloride, prepared in situ from SOCl2 and DMF, to dehydrate formamides. This procedure is applicable in the preparation of aliphatic, alicyclic, vinylic, and aromatic isonitriles. The reduction of isocyanates with LiAlH(OBu-tert)3 to formamides was described.
IT **32529-00-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 32529-00-3 CAPLUS
CN Urea, N-formyl-N,N'-bis(1-methyl-2,2-diphenylcyclopropyl)- (9CI) (CA INDEX NAME)



L3 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1966:468519 CAPLUS
DN 65:68519
OREF 65:12792c-e
TI Cytokinin activity of some substituted ureas and thioureas
AU Bruce, M. I.; Zwar, J. A.
CS Div. Plant Ind., C.S.I.R.O., Canberra, Australia
SO Proc. Roy. Soc. (London), Ser. B. (1966), 165(999), 245-65
DT Journal
LA English
AB N,N'-Diphenylurea had reproducible cytokinin activity. N-Monosubstituted and N,N'-disubstituted ureas (500) were examined, and .apprx.250 were active. The following generalizations were made with regard to the correlation of chemical structure with biol. activity: (1) phenylurea was the simplest active compound; (2) an HNCONH bridge conferred higher activity than an HNCSNH bridge; (3) compds. in which both amino H atoms on 1 or both sides of the bridge were substituted were of low activity or were inactive; (4) ring substitution on the bridge (RNHCONH2, R = substituted phenyl ring) increased the activity, and meta substitutions gave highest activity, while ortho substitutions gave lowest activity; (5) compds. with electron-attracting substituents were more active than those with electron-donating substituents; (6) pyridyl compds. were active, but compds. with non-planar rings were inactive; and (7) in compds. of the type RNHCONHR', where R and R' were phenyl or substituted phenyl groups, compds. having 1 unsubstituted phenyl ring had higher activities than those having 2 substituted phenyl groups. Some ureas showed detectable activity at 0.1 ppm., which was .apprx.4-fold less active than kinetin in the tobacco pith assay.
IT **13201-82-6**, Urea, 1,3-bis(2-phenylcyclopropyl)-, trans,trans-
(plant regulator activity of)
RN 13201-82-6 CAPLUS
CN Urea, 1,3-bis(2-phenylcyclopropyl)-, trans,trans- (8CI) (CA INDEX NAME)



L3 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1966:468518 CAPLUS
DN 65:68518
OREF 65:12792b-c
TI Effect of gibberellic acid on growth of woody ground-cover plants
AU Kemmerer, Harleigh; Butler, J. D.
CS Univ. of Illinois, Urbana
SO Proceedings of the American Society for Horticultural Science (1966), 88, 698-702
CODEN: PASHA6; ISSN: 0099-4065
DT Journal
LA English
AB Two-year-old plants of Euonymus fortunei coloratus, Vinca minor, Celastrus scandens, and Juniperus horizontalis plumosa were sprayed with gibberellic acid at 1 application of 100 and 1000 ppm., and 100 ppm. weekly, over 3 months. Some of the treatments stimulated shoot production. Treated V. minor developed chlorosis that could not be overcome with addnl. fertilizer or chelated Fe. The chlorotic foliage eventually died. Juniper plants also were injured by the sprays.
IT **13201-82-6**, Urea, 1,3-bis(2-phenylcyclopropyl)-, trans,trans-
(plant regulator activity of)
RN 13201-82-6 CAPLUS
CN Urea, 1,3-bis(2-phenylcyclopropyl)-, trans,trans- (8CI) (CA INDEX NAME)



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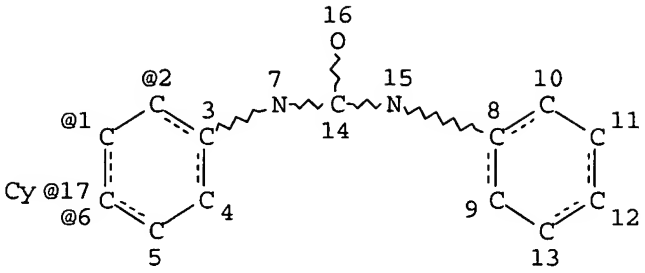

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

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FULL ESTIMATED COST	163.48	163.69

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 29 Jun 2005 VOL 143 ISS 1
FILE LAST UPDATED: 28 Jun 2005 (20050628/ED)

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This file contains CAS Registry Numbers for easy and accurate

substance identification.

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L8            5 L7

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L8   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:1127328  CAPLUS
DN   142:74457
TI   Preparation of ureidocyclohexylmethylpiperidines as modulators of
     chemokine receptor activity.
IN   Delucca, George V.; Ko, Soo S.
PA   Bristol-Myers Squibb Company, USA
SO   PCT Int. Appl., 140 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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PI   WO 2004110993         A2    20041223    WO 2004-US20006          20040612
     WO 2004110993         A3    20050217
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             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRAI US 2003-478022P      P     20030612
OS   MARPAT 142:74457
GI
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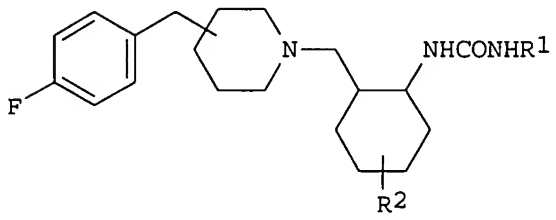

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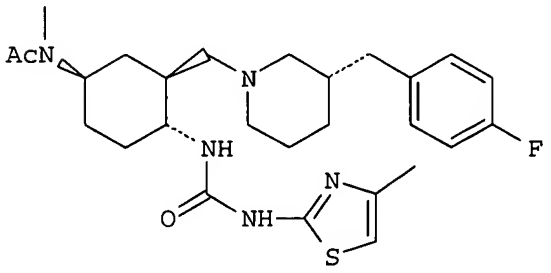


II

AB Title compds. [I; R1 = alkyl, (substituted) carbocyclyl(alkyl), heterocyclyl(alkyl); R2 = N(R4a)2, NR4fCHO, NR4fCO2R4b, NR4fCO(CHR')rR4b, etc.; R4a = H, alkyl, alkenyl, alkynyl, (substituted) carbocyclyl(alkyl),

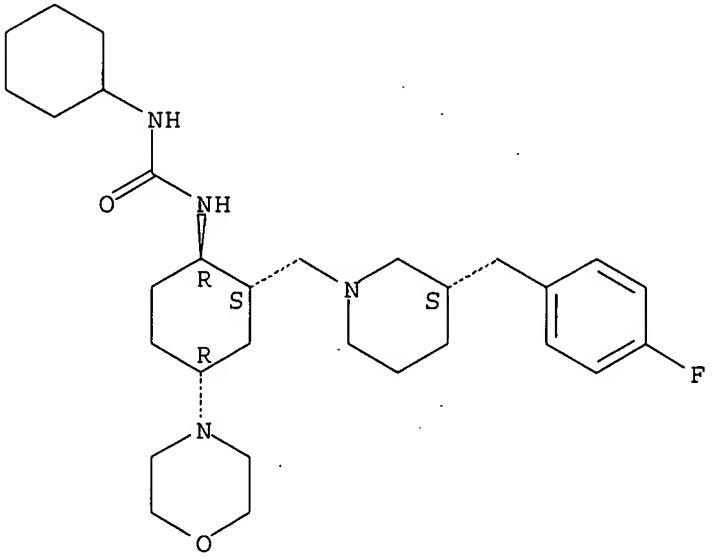
heterocyclyl(alkyl); (R4a)2, R4bR4f = atoms to form a 5-7 membered (substituted) heterocyclyl; R4b = alkyl, alkenyl, alkynyl, perfluoroalkyl, (substituted) carbocyclyl(alkyl), heterocyclyl(alkyl); R4f = H, alkyl, cycloalkyl, Ph; r = 0-5], were prepared as e.g. CCR-1 and CCR-3 chemokine receptor inhibitors (no data). Thus, title compound (II) was prepared in many steps from 1,4-cyclohexanedione monoethylene ketal, (S)-3-(4-fluorobenzyl)piperidine, methylamine, Ac2O, 2-amino-4-methylthiazole, and Ph chloroformate.

IT **813443-85-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ureidocyclohexylmethylpiperidines as modulators of chemokine receptor activity)

RN 813443-85-5 CAPLUS

CN Urea, N-cyclohexyl-N'-[(1R,2S,4R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]-4-(4-morpholinyl)cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:1127098 CAPLUS

DN 142:74455

TI Preparation of ureidocyclohexylmethyl(fluorobenzyl)piperidines as modulators of chemokine receptor activity.

IN Ko, Soo S.; Delucca, George V.

PA USA

SO U.S. Pat. Appl. Publ., 45 pp.
CODEN: USXXCO

DT Patent

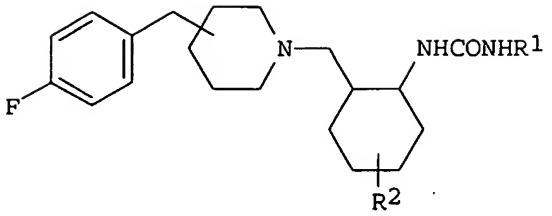
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004259914	A1	20041223	US 2004-865417	20040610
PRAI	US 2003-478022P	P	20030612		

OS MARPAT 142:74455

GI



I

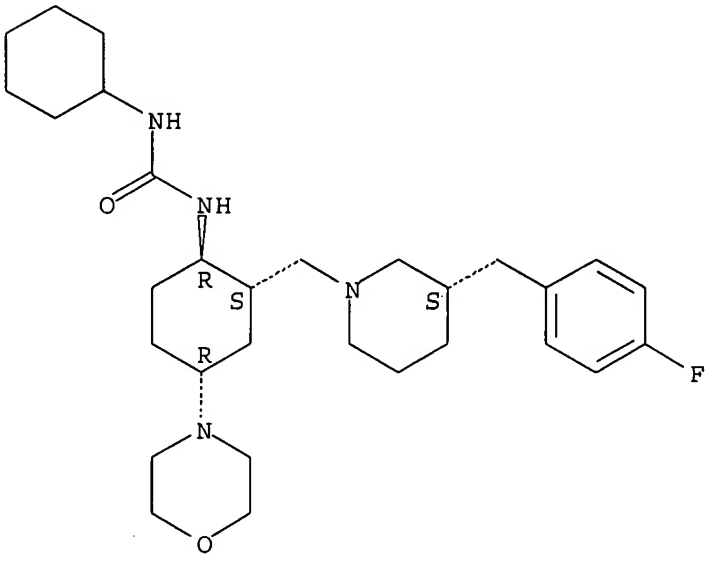
AB Title compds. [I; R1 = alkyl, (substituted) carbocyclyl(alkyl), heterocyclyl(alkyl); R2 = (substituted) amino, acylamino], were prepared as CCR1 and CCR3 inhibitors (no data). Thus, N-(1S,2R,5R)-[4-[3-(4-fluorobenzyl)piperidin-1-ylmethyl]-3-[3-(4-methylthiazol-2-yl)ureido]cyclohexyl]-N-methylacetamide was prepared in many steps from 3-ethoxy-2-cyclohexenone, di-Et carbonate, (S)-3-(4-fluorobenzyl)piperidine mandelate salt, methylamine, and (4-methylthiazol-2-yl)carbamic acid Ph ester.

IT **813443-85-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ureidocyclohexylmethylpiperidines as modulators of chemokine receptor activity)

RN 813443-85-5 CAPLUS

CN Urea, N-cyclohexyl-N'-[(1R,2S,4R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]-1-piperidinyl]methyl]-4-(4-morpholinyl)cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:472724 CAPLUS

DN 135:76865

TI Preparation of N-(isoxazoloquinolinylcyclohexyl)carboxamides and analogs as MRP1 inhibitors

IN Bonjouklian, Rosanne; Cohen, Jeffrey Daniel; Gruber, Joseph Michael; Johnson, Douglas Webb; Jungheim, Louis Nickolaus; Kroin, Julian Stanley; Lander, Peter Ambrose; Lin, Ho-shen; Lohman, Mark Christopher; Muehl, Brian Stephen; Norman, Bryan Hurst; Patel, Vinod Francis; Richett, Michael Enrico; Thrasher, Kenneth Jeff; Vepachedu, Sreenivasarao; White, Wesley

Todd; Xie, Yongping; York, Jeremy Schulenburg; Parkhurst, Brandon Lee

PA Eli Lilly and Co., USA; Wang, Qiuping; et al.

SO PCT Int. Appl., 381 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001046199	A1	20010628	WO 2000-US32443	20001211
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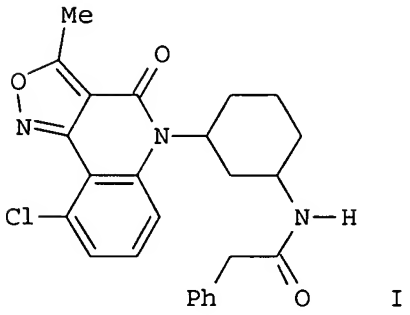
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2395513	AA	20010628	CA 2000-2395513	20001211
	EP 1250340	A1	20021023	EP 2000-986242	20001211
	EP 1250340	B1	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003518125	T2	20030603	JP 2001-547109	20001211
	AT 282623	E	20041215	AT 2000-986242	20001211
	US 2003100576	A1	20030529	US 2002-130800	20020521
	US 6743794	B2	20040601		
	US 2004176405	A1	20040909	US 2004-797362	20040310
PRAI	US 1999-171373P	P	19991222		
	US 2000-226076P	P	20000817		
	US 2000-234539P	P	20000922		
	WO 2000-US32443	W	20001211		
	US 2002-130800	A3	20020521		

OS MARPAT 135:76865

GI



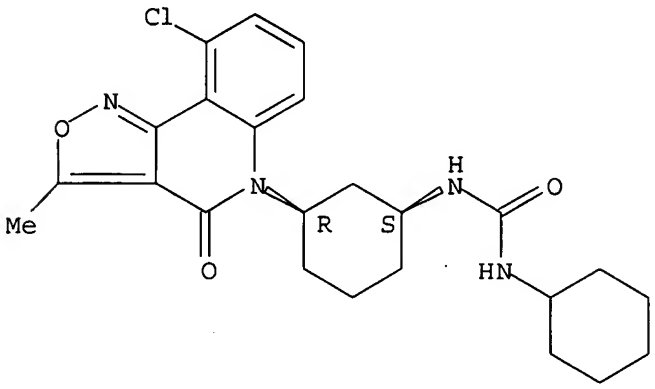
I

AB Title compds. were prepared as MRP1 inhibitors (no data). Thus, mono-N-protected cyclohexane-1,3-diamine was amidated by 3-(2-chloro-6-fluorophenyl)--5-methylisoxazole-4-carbonyl chloride and the cis-product cyclized to give, after deprotection and amidation, title compound I.

IT **347183-19-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of N-isoxazoloquinolinylcyclohexylcarboxamides and analogs as

MRP1 inhibitors)
RN 347183-19-1 CAPLUS
CN Urea, N-[(1R,3S)-3-(9-chloro-3-methyl-4-oxoisoxazolo[4,3-c]quinolin-5(4H)-yl)cyclohexyl]-N'-cyclohexyl-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1965:462817 CAPLUS
DN 63:62817
OREF 63:11461b-h,11462a-b
TI Aryltetralins
IN Rutschmann, Juerg; Schreier, Emil
PA Sandoz Ltd.
SO 32 pp.
DT Patent
LA Unavailable
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR M3101		19650310	FR	
	GB 1046234			GB	
PRAI	CH		19620830		

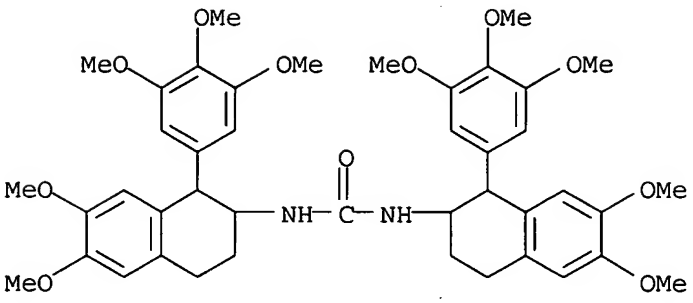
GI For diagram(s), see printed CA Issue.
AB I (R' = CO2Me) (20 g.) is hydrogenated at room temperature on a 10% Pd charcoal catalyst in 300 ml. AcOH to give II (R' = CO2Me), m. 157-8°. II (R' =CO2Et), is obtained by the same procedure. A suspension of 10 g. II (R' = CO2Me) [or II (R' = CO2Et)] is refluxed in 25ml. anhydrous NH2NH2 at 130° for 4 hrs. to give 7.4 g. II (R' = CONHNH2), m. 188-9°. II (R' = CONHNH2) (4.g.) is dissolved in a mixture of 15 ml. 2N HCl and 25 ml. AcOH. The mixture is diazotized and the crude azide is refluxed for 2 hrs. in a mixture of 20 ml. toluene and 5 ml. benzyl alc. to give the corresponding benzyl urethan, m. 182-3°. This compound is treated with H on a Pd-charcoal catalyst in AcOH to give II (R' = NH2); m. 152-3°; HCl salt m. 274-5°. II (R = NH2) (5 g.) is left overnight at room temperature in a mixture of 50 ml. MeOH and 5 ml. ethylene oxide and the solution is further heated at 60° for 2 hrs. to give II [R' = N(CH2CH2OH)2], m. 208-9°, which is heated at 60° for 1 hr. with 5 ml. SOCl2 in 50 ml. CH2Cl2 while stirring to give crude II [R' =N(CH2CH2Cl)2].HCl, which is converted into the free base, m. 140-1°; HCl salt m. 208-9°. Similarly are prepared the following compds. (R' and m.p. given): III: CO2Et, 110-11°; CONHNH2, 178-9°; benzylurethan, 178-9°; methyl urethan, 190-1°; NH2, 109-11° (HCl salt m. 278-80°);

N(CH2CH2OH)2, 86-7°; N(CH2CH2Cl)2, 123-4° (HCl salt m. 210-12°); IV: CONHNH2, 158-9°; benzyl urethan, 147-8°; NH2.HCl, 252-3°; N(CH2CH2OH)2, 95-6°; N(CH2CH2Cl)2.HCl, m. 166°; V: CO2Me, 146-7°; VI: CO2Me, 98-100°; CONHNH2, 178-80°; benzyl urethan, 175-6°; NH2, 151-2° (HCl salt m. 273-4°); N(CH2CH2OH)2, 114-15°; N(CH2CH2Cl)2, 113-14° (HCl salt m. 195-7°); VII: CO2Me, 72-3°; CONHNH2, 150-1°; benzyl urethan, 119-20°; NH2, 67-8° (HCl salt 280-1°); N(CH2CH2OH)2, 134-5°; N(CH2CH2Cl)2, 80-1°; VIII: CO2Me, 119-20°. Compound, X, R2, R3, R4, R5, R6, R7; I, CO, H, --OCH2O--, MeO, MeO, MeO, II, CH2, H, --OCH2O--, MeO, MeO, MeO; III, CH2, H, MeO, MeO, MeO, MeO, MeO; IV, CH2, MeO, MeO, MeO, MeO, MeO, H; V, CO, H, MeO, MeO, MeO, MeO, H; VI, CH2, H, MeO, MeO, MeO, MeO, H; VII, CH2, H, H, H, H, H, H; VIII, CO, H, H, H, H, H; Diazotization of III (R' = CONHNH2) gives a product, m. 255-6, putative bis[1-(3,4,5trimethoxyphenyl)-6,7- dimethoxy-2-tetralyl]urea. Preparation of the corresponding hydrochloride gives a compound identical to III (R' = NH2)-HCl. K (36 g.) is dissolved in 500 ml. tertBuOH (IX) by refluxing 3-4 hrs. under dry N. Then a hot solution of 198 g. 3,4,3',4',5'-pentamethoxybenzophenone and 156 ml. (CH2CO2Et)2 in 300 ml. IX is added and the mixture refluxed for 2 hrs. while stirring. The solution is neutralized with 300 ml. 2N HCl and IX is evaporated under reduced pressure. The acidified solution (Congo red) is extracted with ether and the ethereal solution further extracted with 2N aqueous NaOH. This caustic solution is refluxed overnight and 500 ml. CHCl3 is then added. The mixture is acidified with concentrate HCl to Congo red while shaking. The solution is further extracted with CHCl3 to give the Stobbe acid, m. 172-5°. 3,3,3',4',5'-Pentamethoxybenzhydrylidenesuccinic acid (100 g.) is hydrogenated at ambient temperature in 1 l. alcohol over 4 g. Pd/C catalyst. After the absorption of 5.9 l. H the catalyst is filtered off and the crude dihydro Stobbe acid (100 g.) is collected. Crude 3,4,3',4',5'-pentamethoxybenzhydrylsuccinic acid (100 g.) is refluxed in AcCl 2 hrs. Evaporation to dryness leaves a solid which is treated with benzene. The benzene solution is neutralized with a KHCO3 solution and washed. After evaporation of the solvent, the crude anhydride (95 g.) is dissolved in 300 ml. nitrobenzene (X). To the ice cooled solution is added 60 ml. SnCl4 in 100 ml. X and the mixture stirred overnight at room temperature to give 1-(3,4,5-trimethoxyphenyl)-4-oxo-6,7-dimethoxytetralin-2-carboxylic acid (XI), m. 242-3° (MeOH, EtOH). The mother liquor is evaporated under reduced pressure and the residue is treated with AcOEt to give 1-(3,4-dimethoxyphenyl)-4-oxo-5,6,7-trimethoxytetralin2-carboxylic acid (XII), m. 173-4°. In 300 ml. MeOH and 15 ml. concentrated H2SO4, 25 g. XI is refluxed overnight while stirring to give the Me ester (XIII), m. 171-2°. The Et ester m. 144-5° (alc.). The Et ester (XIV) of XH is obtained by the same procedure, m. 132-3°. Catalytic hydrogenation of XIII gives III (R' = CO2Et), while IV (R' = CO2Et) (b0.001 170°) is obtained from XIV. These new compds. are efficient cytostatic and antimitotic agents. They show low toxicity, even after long applications. They can be used in the treatment of some types of leukemias.

IT **3438-07-1**, Urea, 1,3-bis[1,2,3,4-tetrahydro-6,7-dimethoxy-1-(3,4,5-trimethoxyphenyl)-2-naphthyl]-
(preparation of)

RN 3438-07-1 CAPLUS

CN Urea, 1,3-bis[1,2,3,4-tetrahydro-6,7-dimethoxy-1-(3,4,5-trimethoxyphenyl)-2-naphthyl]- (7CI, 8CI) (CA INDEX NAME)



L8 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1964:30712 CAPLUS
DN 60:30712
OREF 60:5408h,5409a-h,5410a-h,5411a-g
TI Natural products inhibiting mitosis. XIV. Synthetic acid hydrazides and nitrogen mustard compounds of the podophyllotoxin series
AU Schreier, E.
CS Sandoz Ltd., Basel, Switz.
SO Helvetica Chimica Acta (1963), 46(7), 2940-65
CODEN: HCACAV; ISSN: 0018-019X
DT Journal
LA German
OS CASREACT 60:30712
GI For diagram(s), see printed CA Issue.
AB cf. CA 59, 11368a. The podophyllotoxin mol. (I) was modified to secure compds. with an improved antimitotic activity-toxicity ratio and with cytostatic activity. One derivative of this type is II, which has recently been introduced into therapeutics under the designation SP-I SANDOZ. The synthesis was now reported of hydrazides of 1,2-trans-1-aryl- and -1-aryl-4-hydroxytetralin-2-carboxylic acids containing alkoxy groups in various positions of the aromatic rings, as well as several nitrogen mustard compds., all being 1,2-trans-compds. instead of the cis variety in the natural series. 1-Phenyl-4-tetralone-2-carboxylic acid (III) (100 g.) suspended in 1 l. MeOH and 100 ml. concentrated H2SO4, and the mixture refluxed and stirred overnight and cooled several hrs. gave 96 g. Me ester (IV) of III, m. 119-20°, IV (50 g.) in 500 ml. AcOH hydrogenated over 6 g. 10% Pd-C at room temperature and atmospheric pressure (vibromixer) gave 44 g. 1-phenyltetralin-2-carboxylic acid Me ester, b0.01 130°, m. 72-3°. 1-(3,4-Dimethoxyphenyl)-4-oxo-6,7-dimethoxytetralin-2-carboxylic acid (V) (60 g.) suspended in 600 ml. MeOH and 60 ml. concentrated H2SO4 and the mixture refluxed and stirred 8 hrs. and cooled several hrs. gave 56 g. Me ester (VI) of V, m. 146-7°. VI (50 g.) in 500 ml. AcOH hydrogenated over 5 g. 10% Pd-C as above gave 1-(3,4-dimethoxyphenyl)-6,7-dimethoxytetralin-2-carboxylic acid Me ester, m. 88-90° (MeOH). Catalytic reduction of 1-(3,4-dimethoxyphenyl)-4-oxo-5,6,7-trimethoxytetralin-2-carboxylic acid (VIa) Me ester gave 94% 1-(3,4-dimethoxyphenyl)-5,6,7-trimethoxytetralin-2-carboxylic acid Me ester, b0.001 170-5°, viscous oil. By the procedure of S. (loc. cit.) were prepared 1-(3,4,5-trimethoxyphenyl-6,7-dimethoxytetralin-2-carboxylic acid Me ester (VII) and the 6,7-methylenedioxy analog (VIII) of VII. VIII (10 g.) suspended in 25 ml. anhydrous N2H4 and the mixture refluxed 4 hrs., cooled, and diluted with EtOH gave 7.5IX (R = H, (R1R2 =) CH2O2,R3 = R4 = R5 = OMe) (X), m. 188-9° (decomposition) (EtOH). The following IX were similarly prepared (R, R1, R2, R3, R4, R5, m.p. given): H, H, H, H, H, H, 148-9° (EtOH); H, MeO, MeO, H, MeO, MeO, 179-80° (decomposition) (EtOH); MeO, MeO, MeO, H, MeO, MeO, 158-9° (EtOH-H2O); H, MeO, MeO; MeO, MeO, MeO (Xa),. 178-9° (decomposition) (CHCl3-EtOH). X (5 g.) suspended in 75 ml. MeOH containing 2.5 ml. AcH and the mixture refluxed 15 min. and cooled several hrs. gave 4.53 g. XI [RR' =) ethylidene] (XII), m.

198-9° (CH2Cl2-MeOH). The following XI were similarly prepared (RR' and m.p. given): dodecylidene, 142-3° (MeOH); isopropylidene, 205-6° (MeOH); benzylidene 222-3° (MeOH). XII (1 g.) dissolved in 50 ml. EtOH by heating, the solution cooled to room temperature, treated with 1 g. NaBH4 in 10 ml. H2O, stirred overnight at room temperature, and worked up gave 0.94 g. XI (R = H, R' = Et) (XIII), m. 199-200° (EtOH). Reduction of XII with LiAlH4 in tetrahydrofuran (THF) or by hydrogenation over Pd-C or Raney Ni in EtOH gave less pure XIII in poorer yields. Similarly was prepared XI (R = H, R' = dodecyl), m. 143-4° (EtOH). X (1 g.), 0.4 ml. PhCH2Cl, and 0.5 g. CaCO3 in 20 ml. MeOH refluxed 2.5 hrs. and worked up gave 155 mg. XI (R = H, R' = CH2Ph), m. 181-2° (EtOH), CH2Cl2-EtOH). X (1 g.), 0.8 ml. PhCH2Cl, and 0.5 g. CaCO3 in 20 ml. MeOH refluxed 24 hrs. and worked up gave 260 mg. XI (R = R' = CH2Ph), m. 156-7° (EtOH). X (1 g.) in 25 ml. EtOH and 5 ml. EtOAc refluxed 2 hrs. with freshly prepared Raney Ni (from 2.5 g. alloy) and worked up gave 810 mg. 2-carboxamide analog of X, m. 211-12° (EtOAc-Et2O, EtOAc). 1 - (3,4,5- Trimethoxyphenyl)- 4- oxo- 5,7- methylenedioxytetralin-2-carboxylic acid (XIV) (8 g.) dissolved in 160 ml. H2O with 12 ml. 2N NaOH with stirring, the solution treated dropwise with 4 g. NaBH4 in 40 ml. H2O under ice cooling, kept overnight at room temperature, and worked up gave 7.5 g. 4-OH analog (XV) of XIV, m. 205-6° (decomposition) (MeOH-EtOAc, Me2COMeOH); from the work up mother liquor was isolated a product, m. 184-6° (decomposition), which was separated by fractional crystallization into XV and an epimer of XV, m. 178-82°. XV (500 mg.) suspended in 100 ml. N H2SO4 refluxed and stirred 2 hrs., cooled to room temperature, and the precipitate (470 mg.) crystallized from CH2Cl2-Et2O gave 350 mg.

1-(3,4,5-trimethoxyphenyl)-6,7-methylenedioxy-1,2-dihydro-2-naphthoic acid (XVI), m. 181-2° (MeOH). XV (500 mg.) in 5 ml. AcOH refluxed 4 hrs. and worked up gave 360 mg. XVI, m. 180-1° (Et2O, CH2Cl2-Et2O) XV (300 mg.) heated 15 min. at 250° and distilled in vacuo gave 250 mg. XVI, b0.001 220°, m. 179-80° (Et2O-petr. ether, Et2O). Me ester (XVII) of XVI (via Et2O-CH2N2) m. 138-9° (MeOH). XV (1 g.) with Et2O-CH2N2 gave 905 mg. Me ester (XVIII) of XV, m. 180-1° (MeOH). XVIII (1 g.) suspended in 20 ml. N NaOH and the mixture refluxed and stirred 3 hrs. and worked up gave 730 mg. XV, m. 201-2° (decomposition) (EtOH, Me2CO). XVIII (250 mg.) kept 20 hrs. at room temperature in 2 ml. pyridine with 1 ml. Ac2O and the solution evaporated in vacuo gave the O-Ac derivative of XVIII, m. 178-9° (MeOH). 4-Oxo derivative of VIII (20 g.) in 400 ml. THF and 200 ml. MeOH treated portionwise with 20 g. NaBH4 with stirring and ice cooling, stirred 2 hrs. at 0-5°, treated dropwise with 280 ml. 2N HCl, and worked up gave 13.25 g. XVIII, m. 180-1° (MeOH); the MeOH mother liquor evaporated in vacuo and the residue (7 g.) chromatographed on silica gel with C6H6 gave XVII and 1.55 g. XIX, m. 218-19° (MeOH, CH2Cl2-MeOH); further elution with CH2Cl2 gave both C-4 epimers of 1-(3,4,5- trimethoxyphenyl) - 4 - methoxy - 6,7 - methylenedioxytetralin -2-carboxylic acid Me ester (XX); the lower melting isomer (XXI) of XX m. 149-50° (MeOH), and the higher melting isomer (XXII) of XX m. 160-1° (EtOH). XVIII (1 g.) suspended in 30 ml. MeOH containing 3 drops concentrated H2SO4 and the mixture refluxed 2.5 hrs. and

worked up gave 420 mg. XXI, m. 150-1° (MeOH); from the MeOH mother liquor were obtained 105 mg. XVII and 45 mg. XXII. XV (2 g.) in 10 ml. pyridine and 5 ml. Ac2O kept 4 hrs. at room temperature and worked up gave 1.4 g. XVγ-lactone (XXIII), m. 196-7° (MeOH). Heating XV with Ac2O gave 40% XXIII. XV (4.02 g.) in 50 ml. dioxane stirred 2 hrs. at room temperature with 2.1 g. dicyclohexylcarbodiimide (DCC) and worked up gave 3.15 g. XXIII, m. 196-7° (MeOH, CH2Cl2-MeOH). 1-(3,4,5-Trimethoxyphenyl)-4-oxo-6,7-dimethoxytetralin- 2-carboxylic acid (XXIV) (S., loc. cit.) (4.16 g.) in 150 ml. H2O containing 6 ml. 2N NaOH treated with 2 g. NaBH4 in 50 ml. H2O 6 hrs. at room temperature and worked up gave 2.76 g. 4-OH analog (XXV) of XXIV, m. 181-2° (decomposition) (Me2CO); Me ester (via Et2OCH2N2) m. 157-8° (MeOH); O-Ac derivative (with Ac2O-pyridine

at 20°) m. 132-3° (MeOH). XXV (1 g.) in 10 ml. Ac2O refluxed 2 hrs. and evaporated in vacuo gave 620 mg. XXV γ-lactone (XXVI), m. 158-9° (MeOH). XXV (1.66 g.) in 25 ml. dioxane treated with 0.83 g. DCC in 5 ml. dioxane 2 hrs. at room temperature and worked up gave 1.29 g. XXVI, m. 159-60° (MeOH). VIa (4.16 g.) in 150 ml. H2O containing 6 ml. 2N NaOH treated with 2 g. NaBH4 in 50 ml. H2O 6 hrs at room temperature, worked up, the product refluxed 1 hr. with 25 ml. Ac2O, and the solution evaporated in vacuo gave 2.1 g. γ-lactone of 4-OH analog of VIa, m. 152-3° (Et2O, CH2Cl2-Et2O, MeOH). XVIII (10 g.), 100 ml. MeOH, and 20 ml. anhydrous N2H4 refluxed 1 hr. and cooled gave 8.4 g. XXVII (R = NH2, R1 = H, (R2R3 =) CH2O2, R4 = R5 = R6 = MeO) (XXVIII), m. 232-3° (decomposition) (EtOH). XXIII (1 g.), 25 ml. MeOH, and 2 ml. anhydrous N2H4 refluxed 1 hr. and cooled gave 0.8 g. XXVIII. Similarly were prepared XXVII (R = NH2, R1 = R2 = R3: R5 = R6 = MeO, R4 = H), m. 192-3° (decomposition) (MeOH), and XXVII (R = NH2, R1 = H, R2 = R3 = R4 = R5 = R6 = MeO),. 229-30° (decomposition) (EtOH-H2O). XXVIII (1 g.), 15 ml. MeOH, and 0.5 ml. AcOH refluxed 15 min. and cooled gave 985 mg. XXVII (R = N:CHMe, R1 = H, (R2F3 =) CH2O2, R4 = R5 = R6 = MeO) (XXIX), m. 200-2° (decomposition) (MeOH). From XXIII were similarly prepared the following alkylidene derivs. (alkylidene group and m.p. given): dodecylidene, 174-5° (decomposition) (EtOH); isopropylidene, 212-13° (MeOH); benzylidene, 214-15° (EtOH). XXIX (1 g.) in 50 ml. 90% EtOH stirred 2 hrs. at room temperature with 1 g. NaBH4 and worked up gave 860 mg. ethylhydrazide analog of XXIX, m. 221-2° (decomposition) (MeOH, CHCl3-MeOH). To 4.16 g. Xa in 15 ml. 2N HCl and 2N cc. AcOH, 10 ml. N NaNO2 was added dropwise with cooling; after 10 min. the solution was poured on 200 g. ice and worked up, and the crude azide in 20 ml. PhMe refluxed 2 hrs. with 5 ml. PhCH2OH to give 4.2 g. XXX (R = H, R1 = R2 = R3 = R4 = R5 = MeO) (XXXI), m. 178-9° (EtOH). The following XXX were similarly prepared (R, R1, R2, R3, R4, R5, and m.p. given): H, H, H, H, H, H, 119-20° (Et2O) and 109-10° (EtOH); H, MeO, MeO, H, MeO, MeO, 175-6° (CHCl3EtOH); MeO, MeO, MeO, H, MeO, MeO, 147-9° (EtOH); H, (R1R2 =) CH2O2, MeO, MeO, MeO, 182-3° (CHCl3-EtOH). XXXI in 75 ml. AcOH hydrogenated over 100 mg. 10% Pd-C at room temperature and atmospheric pressure (hydrogenation was rapid), and the mixture worked up gave 2.85 g. XXXII (R = H, R1 = R2 = R3 = R4 = R5 = MeO) (XXXIII), b0.001 180°, m. 109-11° (MeOH-2O) HCl salt m. 278-80° (decomposition) (H2O); N-Ac derivative m. 204-5° (EtOH), H maleate m. 198-9° (decomposition) (Me2CO); N-Bz derivative m. 240-1° (CH2Cl2-MeOH). Xa (4.16 g.) converted to the azide as above, the crude azide refluxed 3 hrs. in 20 ml. MeOH, and the solution concentrated gave 3.55 g. Me urethan analog (XXXIV) of XXXI, m. 190-1° (CHCl3--EtOH). XXXIV (2 g.) in 40 ml. EtOH and 40 ml. 40% aqueous NaOH refluxed overnight and worked up gave 320 mg. XXXIII, m. 109-11°. Xa converted to the azide as above, the acidic aqueous solution of the azide added to 250 ml. boiling 2 N HCl, and the whole boiled and stirred 15 min. and worked up gave 1.7 g. putative N,N'-bis [1-(3,4,5-trimethoxyphenyl)-6,7- dimethoxy-2-tetralyl]urea, m. 255-6° the mother liquor gave 1.8 g. XXXIII.HCl, m. 277-9° (H2O). The following XXXII were prepared (R, R1, R2, R3, R4, R5, m.p., m.p. HCl salt, and m.p. N-Ac derivative given): H, H, H, H, H, H, 67-8° (petr. ether), 280-1° (decomposition) (EtOH), 175-6° (EtOH); H, MeO, MeO, H, MeO, MeO, 15-2° (EtOH), 270-2° (decomposition) (H2O-EtOH), 224-5° (EtOH-H2O); MeO, MeO, MeO, H, MeO, MeO, 101-2° (EtOH-Et2O), 252-3° (decomposition) (EtOH), 191-2° (EtOH); H, (R1R2 =) CH2O2, MeO, MeO, MeO, 152-3° (EtOH), 274-5° (decomposition) (H2OEtOH), 227-8° (EtOH-H2O). XXIII (15 g.), 150 ml. MeOH, and 15 ml. ethylene oxide kept overnight at room temperature and 2 hrs. at 60° in a closed vessel and worked up gave 92% XXXIV (R = H,R1 = R2 = R3 = R4 = R5 = MeO)(XXXV),m.

107-8° (Et2O); methanolate m. 86-7°(MeOH). XXXV (0.8 g.), 5 ml. pyridine, and 3 ml. Ac2O kept overnight at room temperature and worked up gave the di-O-Ac derivative of XXXV, b0.001 220°. The following XXXIV were prepared (R, R1, R2, R3, R4, R5, m.p., and b.p./mm. of di-O-Ac derivative given): H, H, H, H, H, H, 133-4° (MeOH), -; H, MeO, MeO, H, MeO, MeO, 114-15° (CH2Cl2Et2O), -; MeO, MeO, MeO, H, MeO, MeO, 95-6° (CH2Cl2Et2O), 225-30°/0.001; H, (R1R2 =) CH2O2, MeO, MeO, MeO, 208-9° (EtOH), 215°/0.001. XXXV (15 g.) and 10 ml. SOCl2 in 150 ml. CH2Cl2 heated and stirred 1 hr. at 60° and the solution evaporated in vacuo gave 16.1 g. XXXVI (R = H, R1 = R2 = R3 = R4 = R5 =

MeO) HCl salt (XXXVII.HCl), m. 210-12° (decomposition) (Me2CO). XXXVII.HCl (15 g.) gave 12.3 g. XXXVII, m. 123-4° (MeOH). The following XXXVI were prepared (R, R1, R2, R3, R4, R5, m.p., and m.p. HCl salt given): H, H, H, H, H, H, 80-1° (petr. ether), -; H, MeO, MeO, H, MeO, MeO, 113-14° (Et2O), 196-8° (decomposition) (MeOH-Me2CO); MeO, MeO, MeO, H, MeO, MeO, -, 166° (decomposition) (EtOAc); H, (RR2 =) CH2O2, MeO, MeO, MeO, 139-40° (Me2CO-MeOH), 205-6° (decomposition) (EtOH-Me2CO). Most of the new compds. were used in orientation studies for cytostatic activity. Of the investigated IX, XI, XXVII, XXXII, and γ-lactones of 1-aryl-4-hydroxytetralin-2-carboxylic acids, only the 6,7-methylene-3',4',5'-trimethoxy-substituted representatives exhibited a significant inhibiting action of cell division in in vitro tests with P-815 mastocytoma cell cultures. The XXXVI cell showed a strong inhibition of cell increase in cell cultures with mouse ascites tumor. Results of other pharmacol. tests, as well as infrared and ultraviolet spectral data, were given.

IT **3438-07-1**, Urea, 1,3-bis[1,2,3,4-tetrahydro-6,7-dimethoxy-1-(3,4,5-trimethoxyphenyl)-2-naphthyl]-
(preparation of)

RN 3438-07-1 CAPLUS

CN Urea, 1,3-bis[1,2,3,4-tetrahydro-6,7-dimethoxy-1-(3,4,5-trimethoxyphenyl)-2-naphthyl]- (7CI, 8CI) (CA INDEX NAME)